ADVANCES IN MILITARY PATHOLOGY DURING THE PAST FIFTY YEARS

BY

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The fifty years which have elapsed since the formation of the R.A.M.C. in 1898 to the present day is a long time in the measurement of scientific achievement so that any survey of the advance in Military Pathology during that period must, of necessity, be in the nature of a series of rather incomplete sketches, if such an account is to be of reasonable length. Two world wars have profoundly influenced this advance in a way no other circumstance possibly could. New problems demand new techniques in pathology as in any other science, new diseases demand new methods of diagnosis and attack, and new methods of waging war require most careful study and preparation, if we are to guard against them as we ought to do. In considering these advances, too, and the manner in which they were made, we must recollect that, in the early days of the Corps, research in pathology (as in other branches of medicine) was organized somewhat differently from to-day; neither the Medical Research Council nor its forerunner the Medical Research Committee was in being, so that effort in research tended to be somewhat more individual than it is to-day, though urgent problems such as that presented by the ravages of Malta fever and sleeping sickness called for a combined effort resulting in the formation of Commissions of the Royal Society to attack the problem and solve it. Finally, in a review over such a period of time it is only too easy to give undue prominence to one part of it at the expense of another, or to one aspect of pathology to the detriment of others equally or even more important; for example, from the very nature of the duties of the Corps, much of our survey must lie in the realms of tropical medicine and pathology which may, therefore, seem to receive undue attention.

EARLY DAYS

Military pathology was, of course, built on firm foundations many years before the formation of the Royal Army Medical Corps and many famous members of the Medical Staff Corps and Indian Medical Service were trained at the Army Medical School at Netley prior to 1898. At the beginning of our era, Dr. (later Sir) Almroth Wright was Professor of Pathology at the Army Medical School—an appointment which he had held since his return from Australia in 1892. It was during this period at Netley, while giving instruction to one-time surgeons-on-probation—now for the first time officers of the R.A.M.C.—that he pursued his epoch-making work on anti-typhoid vaccination. In 1898, a trial of the vaccine was first instituted on a fairly large scale in volunteers in the British Army in India, and in the following year no less than 30,000 men were inoculated against typhoid fever on board ship, the majority being en route for South Africa. Wright's assistant and able collaborator at this time was Major A. D. Semple, R.A.M.C., shortly to become the
first Director of the Pasteur Institute of India, Kasauli, which had the distinction of being the first of its kind in the British Empire. Another member of this pathology team at Netley, because it was a team in the real sense, was Captain W. B. Leishman, R.A.M.C., who, on his return from India in 1897, was posted to the Victoria Hospital and soon entered enthusiastically into all the work going on in Wright's laboratory, including that pertaining to antityphoid inoculation and investigations into Brucella infections. In 1900, Leishman succeeded Semple as Assistant Professor of Pathology and it was very soon after this that he made his first original contribution to medical literature in his article on "A method of obtaining rapid Romanowsky staining by a single solution" published in the *British Medical Journal* (1901). The stain is known as Leishman's stain the world over, and has been used successfully by thousands of clinicians and pathologists ever since. The method surpassed those previously employed, in not requiring preliminary fixation of the blood-film, in being very much more rapid—five to ten minutes instead of two hours or more, and in not giving a deposit on the film. It would indeed be difficult to overestimate the influence of the Army Medical School on the course of tropical pathology and medicine in the world at large through the work of men like Bruce, Ross, Leishman, Cummins, Horrocks, Lewis and very many others.

**South African War to First World War**

*Enteric Group Fevers.*—Recollection of the South African War by the epidemiologist at once evokes thoughts on typhoid fever, as this disease occasioned no less than 57,684 admissions to hospital and 8,020 deaths in a force of 208,000 men. There were, in fact, many more admissions than this, because at that time a number of the milder cases of enteric fever were listed under the term "Simple Continued Fever" and were recorded as such. The diagnosis of "Continued Fever" included enteric fever and simple continued fever and the differentiation between these two conditions is difficult. It is essentially a matter for laboratory diagnosis. At the time of the South African War (and in fact for too many years afterwards) the importance to the Army of a properly organized Pathological Service with central direction was not recognized, so that a fully functioning laboratory service was not generally available. It is true that a General Hospital had a laboratory but its scope can be gauged from its equipment table, which stated "Instruments, appliances, drugs, etc., necessary for Pathological and Bacteriological Laboratory—Regulation Allowance NIL—Required 1—all to be packed in one case complete." When bacteriological investigation was made into cases of so-called "simple continued fever" many proved in reality to be cases of "larval, abortive and extremely irregular enteric fever," as we would expect. Blood culture was not then the routine diagnostic laboratory procedure of choice it has since become in the Army of to-day. Nor, was the real danger of the "healthy carrier" in the spread of enteric fevers and other infectious fully appreciated at the time. More attention was given to "soil and water" and even to aerial contamination, as possible sources of infection; for example, in the Report of the Health of the Army for 1900, "emanations" arising from a neighbouring prisoner-of-war camp
occupied by Boers was suggested as the cause of an outbreak of typhoid fever in the 2nd Kings Royal Rifles, who were doing guard duties. The continuous and original research of many officers of the R.A.M.C. in India and elsewhere at this time contributed greatly to the advance in laboratory methods of diagnosis of enteric group infections. Mention has already been made of the introduction of Wright’s inoculation against typhoid fever, but the numbers inoculated in South Africa were relatively too few for a correct assessment of the value of this procedure. That advance had to wait for some years.

Dysentery was responsible for 38,000 admissions and 1,342 deaths in the South African War and was secondary only to enteric fever as a loss of manpower. At this time, the dysenteries were classified as endemic, epidemic and sporadic, and it was recognized that epidemics were normally bacillary in origin. None the less, bacteriological investigation of bacillary dysentery was very much in its infancy as Shiga first described his bacillus in 1898 and Flexner described his strains only in 1901. It is difficult to appreciate now, that fifty years ago the causation of tropical abscess of the liver had not, in fact, been traced to Entamoeba histolytica and that medical treatment of the condition was non-specific. Case-records of tropical abscess of the period with their accounts of repeated attacks of dysentery impel regret that the etiology of the condition had not then been discovered.

Leishmaniasis.—The finding of a new protozoon in the spleen of a soldier suffering from “Dum-dum fever” by Major W. B. Leishman, R.A.M.C., was one of the most interesting and important discoveries of the early twentieth century. One must pay tribute to the keen observation which enabled Leishman to detect these minute bodies in the splenic pulp. There can be little doubt too, that an excellent staining technique contributed to his success because at this time he was working on the Romanowsky stains, and was to publish his note on his method of staining in the following year (1901). Leishman thought at first that these bodies might be fragmented nuclei of trypanosomes and did not place his observations on record till some three years later. Some time after, in the Army Medical School, Wright found Leishman-Donovan bodies in the lesions of “tropical ulcer” establishing the etiology of this condition. It was not, however, until some time later that successful transmission of kala-azar by the bite of the sandfly was effected by the notable work of members of the Indian Medical Service. The sandfly had been incriminated on epidemiological grounds for many years, as the transmitter of Leishmania infections but it was only during the recent war that this was proved by workers in India who successfully infected volunteers by sandflies, which had been kept alive by a newly discovered method of feeding.

Sleeping Sickness.—The following announcement appeared in the London Gazette of December 18, 1903: “The undermentioned Lieut.-Colonel to be Colonel—David Bruce, F.R.S., M.B., R.A.M.C., in recognition of his services in investigating the cause of ‘Sleeping Sickness’ in Uganda, as well as in consideration of the distinction already attained by him in researches connected with Malta fever and tsetse-fly disease.” This was the first brevet promotion to be awarded for distinction in original research. Our knowledge of medical
trypanosomiasis dates back to the days before the formation of the R.A.M.C. in the discovery of a trypanosome in the blood of rats by Surgeon Major T. Lewis, F.R.S. In 1903 Bruce joined the Commission on Sleeping Sickness already established in Entebbe, Uganda and, with his work on tsetse-fly disease in cattle fresh in his mind, was quick to appreciate the great significance of Castellani's discovery of a trypanosome in the cerebrospinal fluid of cases of sleeping sickness, seized upon it and pursued it in collaboration with Castellani to whom Bruce was the first to give credit for the discovery of the parasite.

Other members of the Corps working under Bruce at this time in the Sleeping Sickness Commission were Captains Hamerton and Bateman. Finally, we must pay tribute to the memory of Lieutenant Forbes Tulloch, R.A.M.C., another member of the Commission, who was infected with trypanosomiasis in Uganda and died of a virulent form of sleeping sickness in London in June 1906. Published works of the Commission included studies on the development of *T. gambiense* in *Glossina palpalis*, on trypanosomes found in the blood of wild animals, and on trypanosomes as a cause of disease in domestic animals. They found time, moreover, to study a disease of the native known as "Mukinyo" which proved to be undulant fever, and a disease of cattle known as "Amakele," which was, in fact, the same as East Coast fever and was due to the presence of a piroplasma in the blood.

**Brucellosis.**—Undulant or Malta fever (now included with contagious abortion in the much more comprehensive term of brucellosis) was a serious drain on the man-power of Army and Navy in Malta over a period of years. This is not to be wondered at when it is realized that the average duration of an attack is four months. Little advance had been made in the control of the disease since the discovery of the organism by Bruce in 1887, its method of entry into the body having defeated all attempts at solution. Wright and Semple of the Army Medical School by means of the agglutination test did much to demonstrate that the distribution of the disease extended widely beyond the confines of Malta and Mediterranean, and to differentiate this infection from enteric, malaria, and other specific fevers. But as late as 1904 no one had found the parasite in "external nature."

There were various theories on the mode of entry of the organism into the human body; at one time drinking water was blamed, and at another time a biting fly was thought to be responsible, but neither theory fitted in correctly with the epidemiology of the disease in Valetta. In the *Journal of the Royal Army Medical Corps* of May, 1904, a plea was made for the appointment of a Commission of whole-time officers to attempt to elucidate the method of infection of this disease which was responsible for so much sickness and invaliding in both the Navy and Army. Whether as a result of this or not, a Commission was appointed in the same year with Bruce as President and, in the following year, the problem was solved by the discovery that the goat was a highly susceptible animal. Prior to this, the goat had been presumed immune and in no way involved in the spread of the disease, because it had not been found possible to infect it with artificial cultures. Agglutination tests proved that *Brucella melitensis* flourished in the goat without producing obvious
symptoms and investigations soon showed that half of the goats in Malta were infected, and that 10 per cent. of them had infected milk. Preventive measures based on these discoveries were impressive in prevention of the disease, and laboratory investigations on similar lines in other parts of the world, elucidated the wide geographical distribution of this infection.

THE FIRST WORLD WAR

In the years preceding the 1914–18 war, the importance to the Army of a well-organized Pathology Service in the diagnosis, prevention and treatment of disease was gradually becoming recognized and the training of regular pathologists had been proceeding steadily, so that the number available at the outbreak of war was more than enough to fill the few pathological posts authorized. But, the need for regular officers to fill field appointments was so great that after six months of war, only four of the regular qualified pathologists remained in the practice of their speciality. The support of civil pathologists and bacteriologists was fortunately forthcoming to fill the ranks of the Pathology Service.

The first anxiety in this war was the unexpected prevalence of tetanus and gas gangrene, and this was one of the early problems faced by Colonel Sir William Leishman on his appointment to the expeditionary force in October 1914, in an advisory capacity.

There were three types of laboratories in the field: (1) Mobile bacteriological laboratories; (2) hospital laboratories; and (3) research laboratories. The mobile laboratory was something entirely new, as bacteriological investigations had never before been carried out so near the front line in any previous war. The first mobile laboratory to go to France in October 1914 was a converted pleasure caravan stripped of all non-essential fittings and fitted with incubators and other apparatus. These laboratories performed a most useful function in the carrying out of routine clinical pathology, carrier tests, and investigations into new and little-known forms of disease such as trench fever, spirochetal fever, gas gangrene and trench nephritis.

Tetanus.—The incidence of tetanus had been negligible in the South African War, but in this war there were approximately 2,529 cases as a result of the fighting in France and Belgium and the incidence was greatest in the early days. Many of us remember seeing these cases of tetanus in the base hospitals of the United Kingdom after the retreat from Mons. Anxiety was great, and the War Office appointed a committee under the chairmanship of Sir David Bruce to investigate the problem. The prompt administration of a prophylactic dose of antitoxic serum to all wounded men will rank as one of the triumphs of the war, not only in reducing incidence but in many cases modifying the course of the disease, when it did occur. It was clearly shown that serum prophylaxis prevented the onset of tetanus completely, in at least five out of six men. Bruce calculated that some two million doses of serum were administered in England alone, and it is worth recording that there were only eleven cases of anaphylactic shock, and not one was fatal.
Gas Gangrene.—The second early cause of anxiety was gas gangrene, which also had been negligible in South Africa. It soon intruded itself in an unpleasant fashion at the battles of the Marne and the Aisne, occurring in 10 to 12 per cent of the wounded. Its aetiology was then unknown, and it rather tended to be looked on as a "hospital infection" until the investigation of Sir Anthony Bowlby and Sydney Rowland in one of the new mobile bacteriological laboratories proved that the gangrene occurring among the wounded was a "traumatic infection" originating at the time of wounding, and was due to the entry of an organism from the soil, and that it was in no way related to sloughing phagedena or so-called "hospital gangrene." It was not, however, until 1918 that antitoxic sera were available for use in the British Army, and then they were limited in scope and not very potent in effect. An efficient method of manufacturing the highly potent polyvalent serum available to us in such generous amount during the recent war, had not then been discovered. But, as a result of the work done at this time it was established that most promise lay in the use of serum in prophylaxis, that the serum should be active against several organisms of the gas-gangrene group, that it should be given as a routine, and that in treatment, serum must be regarded as an adjuvant and not a substitute for efficient surgery.

Wound Sepsis.—The war of 1914–18 provided the first opportunity since the introduction of aseptic surgery, of studying grossly contaminated wounds on a large scale. Suffice it to say that there were two distinct schools of thought and much laboratory and clinical work was expended by both of them. One school placed its faith in "physiological" methods and rejected the use of antiseptics. Sir Almroth Wright was the protagonist of this school. Lorrain Smith and Dakin upheld the second school which trusted more in germicides of one kind or another.

Enteric Group Infections.—The greatly reduced incidence of enteric group infections as compared with the South African War, is one of the outstanding features of the medical history of the war. After making due allowance for the part played by military hygiene and also for the more correct appreciation by the combatant officer and soldier of his share in the practice of hygiene in producing this result, there were two other factors of great importance. One was, of course, the general immunization against enteric group infection, and the other was a more correct appreciation of the danger of the "healthy carrier" in the spread of infection. Antityphoid inoculation had been tried out very tentatively in South Africa, and subsequent work in India under Leishman's direction had demonstrated the value of this procedure. Methods planned in advance were put into practice, and the whole Army was inoculated in a couple of months. In August 1914, only 25 per cent of troops were inoculated before embarking for France but by the end of 1915, due to Leishman's efforts, 98 per cent of troops were protected, and enteric fever which had broken out and spread; started to decline. If the rate had been similar to that in South Africa, there would have been half a million cases and more than 77,000 deaths. Actually, there were 20,000 cases of enteric fever in all theatres of war and 1,191 deaths. Early in 1916, triple T.A.B. vaccine was introduced
to provide protection against the paratyphoid fevers in addition to typhoid fever, with beneficial effect.

It had been known for many years that "carriers" existed, but this knowledge had not been utilized to the full. Pathologists in India and other foreign stations contributed largely in the inter-war period, to a true appreciation of the carrier danger. Methods of detection have greatly improved since then, by the introduction of highly selective culture media, rendering the detection and isolation of typhoid carriers a much more practicable proposition. In the 1914–18 war, the macroscopic agglutination test of Dreyer and the method of serial agglutination tests were widely practised in an attempt to overcome the diagnostic complication of universal T.A.B. inoculation; for many years after, in India and elsewhere, military pathologists strove to evaluate the agglutination test in an inoculated community at its true worth. And, as a result, our knowledge is now on a factual basis and the limitations of the tests correctly understood and applied in medical practice.

**Dysentery—bacillary.**—Initially, on the Western Front, bacillary dysentery was not a problem but, later, Mesopotamia and the Eastern Mediterranean contributed more than their share of this disease. Cases arriving in England were concentrated in special areas, and subjected to careful study, but the knowledge gained was not commensurate with the labour expended. It was not at first appreciated that the case must be studied in the laboratory in the acute stage. But by the summer of 1916, dysentery diagnosis had come to form a considerable part of the work of all laboratories on the Western Front. New techniques in diagnosis were evolved and one of them, the direct microscopic examination of material from the bowel, was an advance of tremendous practical value because in this way the rapid diagnosis of large numbers of cases became a practical proposition. By 1917, there were well-equipped laboratories in all the main theatres of war, and a careful study of the strains of organisms isolated as a result of their work was carried out at the Royal Army Medical College.

**Dysentery—Amoebic.**—Progress in our knowledge was slow at first owing to a scarcity of trained protozoologists, as few pathologists had had any experience of the microscopical examination of stools. But intensive training in the study of protozoology was begun and continued to the end of the war with excellent results. Rapid microscopic diagnosis of the type of exudate was as important as in the case of bacillary dysentery.

**Typhus Fever and Trench Fever.**—The etiological significance of *Rickettsia prowazeki* had been firmly established just before the outbreak of war, but British medical officers had little opportunity of advancing knowledge because they encountered typhus under conditions unsuitable for pathological research. Active immunization was in its early stages and the results of vaccination were inconclusive. Trench fever was not definitely accepted as a rickettsial infection at the end of the war, though it was established that it was transmitted by the body louse and that the blood of trench fever patients might contain the virus for many months. McKee, who had charge of a mobile laboratory, took a large share in the experimental pathology of this disease, and it was through
his efforts that the infectivity of a patient’s blood for man was proved. It was also demonstrated that the virus was contained in the corpuscles, and that clear serum was non-infective. Certain British medical officers carried out some very suggestive experiments on themselves in demonstrating the infectivity of lice. Although the exact nature of the virus had not been established by the end of the war, it was thought to be rickettsial and sufficient knowledge had been acquired for prophylactic measures to be adopted on a rational basis.

Weil’s Disease.—Localized outbreaks of Weil’s disease, particularly in the Ypres Salient in the summer of 1916, provided opportunity for study. It was demonstrated that 30 per cent of the rats in the area were excreting \( L. \text{icterohaemorrhagiae} \) in their urine and that live spirochaetes were present in the urine of convalescent patients for several months after clinical recovery.

Cerebrospinal Fever.—The spread of meningococcal infection amongst the troops training in England during the early months of 1915 occasioned serious concern and, naturally, stimulated intensive study. Any suspected case was visited at once by a trained bacteriologist. A central cerebrospinal fever laboratory was established at the R.A.M.College and laboratories in all commands were equipped as special centres for study.

Our knowledge of the manufacture of suitable culture media for growing this delicate organism and of its antigenic structure were advanced. The “striking distance” of droplet infection, and the co-relation between the anti-endotoxic value of a serum and its therapeutic efficiency were demonstrated. The new information acquired was of value in the prophylaxis of this disease and was of the greatest value in establishing a specific method of treatment in the days before the sulphanamides and penicillin came to our aid. In 1914, it was calculated “that a man attacked by the disease had on the average only one chance in three of escaping death, whether he was a civilian or a soldier... The progressive improvement shown by the military results was due no doubt to early diagnosis and treatment, the proper use of lumbar puncture, and especially in the last year, to the use of an effective serum. In 1918–19 an attacked soldier, if his disease was of Type I and serum was available, was given close to nine chances out of ten of escaping death.” These words are quoted from the Introduction to the Medical Research Council Report on Cerebrospinal Fever 1915–19, and for much of this work we are indebted to Dr. Mervyn Gordon.

Schistosomiasis.—A notable advance in the solution of the Bilharzia problem in Egypt was achieved by Leiper when he demonstrated that the life-cycle of the Egyptian schistosomes followed, in practically all details, that of \( S. \text{japonicum} \) previously elucidated by the Japanese.

**THE INTER-WAR YEARS**

The Pathology Directorate was created in 1919, and Sir William Leishman, who had been Adviser in Pathology first in France and later at the War Office, was appointed first Director of Pathology. The Advisory Committee came into being in the same year and, at its first meeting, the Director intimated that, in his view, it should concern itself rather with fundamental inquiries...
into the origin and prevention of disease than into work of a routine nature in connexion with any one special condition. Antityphoid inoculation was a frequent subject of discussion at the early meetings. In 1926, Manifold reported from India that practically all the dysentery in Poona was bacillary in origin due to the Flexner group of organisms, and that amoebic dysentery was much less common than had formerly been supposed. During this period, a great deal was done in the reconstruction and building of laboratories at home and abroad—particularly in India where new laboratories of excellent construction and good design were built in Commands and Districts, i.e. Meerut, Quetta, Lahore, Secunderabad, etc. Two advances in the field of tropical medicine and pathology during this inter-war period, which were of the greatest importance to the Army, were the discovery of immunization against yellow fever by the Americans and the introduction of atebrin by the Germans.

J. S. K. Boyd's classical work in India on the dysentery bacilli placed our knowledge of the antigenic structure of this group of organisms on a firm basis. He demonstrated the inadequacy of the previous system of classification of the large and important mannitol-fermenting group of organisms based, as it had been, on an unavoidably incomplete collection of dysentery strains, many of which had undergone variation, an unrecognized phenomenon at the time of the original classification. Due to his investigations a scientific classification was made possible. A voluminous amount of work was carried out in this field by pathologists in India and elsewhere.

The Salmonella group of organisms were attaining a new significance as a result of methods of antigenic analysis, and several new strains were added to the growing collection by Major R. F. Bridges, R.A.M.C. The efficacy as a vaccine of the Rawlings strain of *Bact. typhosum*, which had been employed since the time of its first isolation in 1900, as the typhoid component of the antityphoid vaccine of our own and many foreign countries came under suspicion a few years prior to 1934. As a result of a series of investigations at the Royal Army Medical College these suspicions were confirmed and the value of selected virulent typhoid strains in vaccine production was demonstrated. The discovery of the Vi antigen of *Bact. typhosum* by Felix and Pitt, followed in its turn by the discovery of a highly specific Vi bacteriophage by Craigie were incidents of great epidemiological and immunological significance and interest to the military bacteriologist.

1939-1946.—In the recent war, the scope of the pathology service became wider than ever before, due to the rapid advance in subjects within its purview. The service was responsible not only for the supervision of hospital and mobile bacteriological laboratories and for the organization of research in laboratories, but also, in co-operation with Consultants and Advisers in all branches of medicine and surgery, for the scientific control of chemotherapeutic agents, penicillin therapy, immunization procedures, vaccines and sera. In the Blood Transfusion Service alone, the development of which was one continual advance in method and organization, there was scope for almost unlimited work. Research was organized and directed with the help of the Medical Research
Council by the formation of teams designed to work on urgent problems as they arose. Teams to study shock, typhus, anaerobic infection and penicillin control were examples of such research, apart from the continual investigations in many other fields too numerous to mention—common cold, influenza, infective hepatitis, therapeutic trials, effects of immunization, etc., etc. Many of these teams functioned in the field in specially equipped mobile bacteriological laboratories. Central laboratories were established in the Middle East and India and an Emergency Vaccine Laboratory was formed in England. Apart from performing routine work these laboratories constituted highly specialized reference laboratories and centres of instruction, in which research of one kind or another was constantly in progress. It is obvious, therefore, that in this enormous panorama only the barest outlines can be given.

Tetanus.—The incidence of tetanus in the wounded, fighting over the same terrain was less than in the previous war. A ratio of 1.47 per thousand in 1914–18 on the Western Front fell to a ratio of 0.43 per thousand in troops in France in 1939–40, and to a ratio of 0.06 per thousand in 1945 in over much the same ground. The main reason for this comparative immunity is believed to lie in the general active immunization against tetanus which was instituted in 1939. Between the two wars, active immunization against both diphtheria and tetanus was developed. The Army took a very active part in the development of tetanus prophylaxis, and tests on dosage and the optimum interval which should elapse between doses were carried out by Boyd at the R.A.M. College. Immunization prior to proceeding on active service was adopted, and there can be little doubt that it greatly reduced the incidence of tetanus in World War II.

Gas Gangrene (Clostridial Myositis).—The knowledge of the pathology, bacteriology and treatment of gas gangrene gained in 1914–18 was advanced considerably during the recent war. The War Wounds Committee of the Medical Research Council set up in 1942 an anaerobes Sub-Committee of which the Director of Pathology was Chairman, to inquire into the prevention and treatment of anaerobic wound infection, particularly gas gangrene. In addition to directing research, the anaerobes sub-committee was concerned very largely with the rapid propagation of knowledge. Special courses were arranged for Army pathologists in the bacteriology of anaerobes. Information on gas gangrene treated in the United Kingdom was mainly derived from analysis of case reports but very valuable information on anaerobic infections of war wounds was obtained as a result of an investigation by Major J. D. Maclean, R.A.M.C., originating in the Middle-East Force and continuing in Italy and France. Apart from the excellence of the bacteriology, the centralization of the work in one laboratory was clearly of the greatest value in obtaining the maximum information from a comparatively small number of cases. The results of these investigations have, of course, been published and we can only deal with them here very briefly and incompletely. Points of particular interest in this report were the descriptions of infections with Cl. aedematiens, and the description of streptococcal myositis; also the relative importance of the soil and the clothes as sources of infection, the association of proteolytic
organisms, particularly *Cl. histolyticum* with a high mortality rate, and the beneficial effect of antitoxin in treatment. The relationship of the nature of the infecting organisms both to time of onset of the disease and to its mortality was traced by Maclennan. When only one of the pathogenic Clostridia was present the average time of onset was twenty-three hours. The mortality rate tended to rise if more than one of the pathogenic Clostridia or a proteolytic Clostridium, was present, and reached 100 per cent in the presence of *Cl. histolyticum*. Our knowledge and understanding of this grave infection increased substantially during the war so that better methods of prophylaxis and treatment were introduced with improved antitoxins and new drugs to supplement treatment with surgical measures which remains the most important prophylactic measure.

**Penicillin Research.**—The Army penicillin research organization consisted at first of surgeon; bacteriologist and technicians working in the different theatres of war with the limited supplies then available. Reports of both early and late treatment of infected wounds had confirmed the early promise of the value of penicillin. As supplies became more readily available, the laboratory aspects of penicillin investigations in hospitals on active service received widespread attention in hospital laboratories and specialized units. Detailed attention was given to its stability, dispensing, sensitivity, activity alone and in combination with various sulphonamides. Its value in wounds in general, and in head wounds, chest wounds, joint injuries, in particular was a subject of continued study in collaboration with the clinician. Its value in medical treatment was controlled, and different techniques for its estimation in body fluids examined in the laboratory. Penicillin was the object of tremendous attention resulting in great advances which have only been briefly hinted at. Apart from well-organized co-ordinated research for which the war provided a unique opportunity, it is little exaggeration to say that there was scarcely any laboratory at home or abroad in which the pathologist did not devote such time as he could spare at the bench, to the practical study of penicillin in its various aspects.

**Blood Transfusion.**—It would be difficult to imagine any subject in which the advance in knowledge and in practice was so great as in that of blood transfusion. It can only be described as revolutionary. Blood transfusion from being a procedure of frequency only in hospital practice was introduced to front-line units and was given anywhere. Boxes containing dried serum, and crystalloids together with powdered blood-grouping sera, with the apparatus, for the taking and giving of whole blood from local donors, were carried, by all forward medical units, hospital ships, troopships, ambulance trains, etc. These boxes enabled small numbers of transfusions to be undertaken in emergencies when continuous contact with either the Army Blood Supply Depot or a Transfusion Unit was not possible. New products were made, new methods introduced and new units formed to function in their great expansion. The work of the Army Blood Transfusion Service under the direction of Sir Lionel Whitby will live for many years as an example of outstanding achievement in the second world war. Some idea of the volume of work may be
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obtained from the fact that between September 1939 and May 1945 120,817 pints of blood, 342,103 bottles of dried plasma and 345,442 pints of crystalloid solutions were sent out from the Depot and that there were 559,529 individuals on the donor panel for giving blood. It is impossible to detail all the special investigations of the pathology service into transfusion technique, the drying of plasma, manufacture of grouping serum, prevention of shock, etc., etc., which were carried out.

Typhus.—Knowledge of typhus control differed little in 1939 from what it had been at the end of the 1914–18 war, during which millions had died of the disease in central and eastern Europe. And yet the expected holocaust did not occur, though typhus was rife in many battle areas. Africa, Burma, Irak, Persia, Italy were all centres of infection and the menace in Europe was, if anything, intensified on the cessation of hostilities with a devitalized and undernourished people open to attack. What prevented the spread? Undoubtedly DDT and active immunization played the major part. Before and during the war much time was devoted to antigenic analysis of the various typhus Rickettsiae, upon which the principles of immunization and diagnosis both depend. Intensive work was done in the United States and in this country, and not least in the military laboratories at home, in India, Burma, Persia, Irak and Egypt during the war. Strains of Rickettsiae were flown home from the different theatres for study, and antigenic analysis necessary for the preparation of diagnostic material and vaccines. The larva of the mite *Trombicula deliensis* the vector of scrub typhus, which infests localities in South East Asia can be avoided only with difficulty. A special vaccine was prepared against it from the lungs of infected cotton rats. This vaccine had been shown to confer protection on laboratory animals, but the sudden end of hostilities prevented completion of the trial and results were inconclusive: now a new antibiotic—chloromycetin—seems to promise assistance in this field.

Influenza.—Advance in the study of influenza provides a further good example of the beneficial result of co-operation between pathologist and clinician. Cultivation of the virus on the developing chick embryo, the isolation of influenza-B virus and the discovery that influenza virus agglutinated fowl red cells and the fact that this agglutination was specifically inhibited by appropriate immune sera were discoveries of the greatest practical importance in the study of this infection, and in specially equipped laboratories much investigational work was done. Bodies of troops were immunized to study the immunogenic value of influenza vaccine containing viruses A and B, but for lack of adequate opportunity a convincing trial in this country was not forthcoming, and the value of the vaccine remains undetermined.

Infective Hepatitis.—As in the 1914–18 war, so in the recent war, infective hepatitis attacked the armies in the Field, to a degree that is not generally realized—and the Army at home did not entirely escape. The impact of attack was felt very severely in the Middle East Force and Italy. Although many gaps in our knowledge remain, considerable advance was made. So much of this advance was due to combined action that it is invidious to attempt to differentiate the laboratory worker from the clinician. Infective hepatitis
reached epidemic proportions in the Middle-East Force and intensive investigations were made by Cameron and others with the mode of transmission and the discovery of the responsible agent. He demonstrated the artificial communicability of the disease by injecting six human volunteers intravenously with infected blood—all attempts at animal inoculation having proved fruitless. Van Rooyen and Gordon continued investigations into the isolation of a possible virus agent employing in their work a wide range of animals. These tests were also unsuccessful, but various facts emerged such as the immunity of local inhabitants, the significance epidemiologically of subclinical attacks and the liability of officers in the Army (as distinct from the Navy) to contract infection. Following on the discovery of the infective agent in faeces, van Rooyen postulated some lack of acquired herd immunity on the part of officers through less exposure to casual excremental infection an explanation of their increased incidence. This is not generally accepted.

Homologous serum jaundice and the possibility of syringe-transmitted infection became a serious problem in connexion with transfusion of plasma and in arsenerotherapy. It was suggested by Biggar and also by MacCallum that hepatitis was being conveyed through venepuncture and intravenous injections. It soon became evident through the work of Sheehan, Salaman and others that this hypothesis was correct.

Diphtheria.—Although diphtheria never reached serious epidemic proportions it naturally received much study and special interest, because it was always present in the forces. Following on a really intensive immunization of children in 1940, the subject of mass immunization of the troops against diphtheria was continually under review, particularly in the Middle-East Force, where the incidence had been high in certain units. But the work of Boyd on the reaction in the adult resulting from the injection of A.P.T. clearly showed that position of young children and soldiers in a force, was not at all comparable and that more harm than benefit would accrue from blind mass immunization of an adult Army in the Field and that, in any case, it was unnecessary in view of a process of natural immunization during the preliminary years of army communal life. On the other hand, immunization of the recruit as now practised is a well worth-while procedure as a long-term policy.

New bacteriological methods of supplementing cultures on Loeffler slopes by culture on blood-agar media containing potassium tellurite was widely practised in all laboratories and resulted in a much higher degree of accuracy. The role of C. diphtheria in wounds received much study and led to the conclusion that it was a secondary invader only, and not a primary agent and that it was present mainly when infection elsewhere was also present.

Bacillary Dysentery.—Shiga infections were not uncommon and it was noted in the Middle East that the ordinary concentrated antitoxin did not have any marked therapeutic effect. Trials of a new specially refined antitoxin were initiated but the introduction of the treatment of bacillary dysentery by the sulphonamide preparations in adequate dosage, were little less than dramatic and in a short time outmoded any other form of treatment.

India.—A word or two more must be said about work in India where, for
example, the service expanded from a total of 27 laboratories in 1938 to a total during the war of over 120 laboratories spread all over India and the Burma theatre of operations. In addition, laboratories which had been raised in India served in the Middle East, Italy, Irak and Persia. The Central Military Pathology Laboratory was constantly engaged in training pathologists to fill places created by the expanding service, and by its Departments of Histopathology, Bacteriology and Serology and Biochemistry was able to give a full consultative service when required. The pool of research workers investigated many urgent problems and valuable work was carried out by these teams with problems connected with scrub typhus, tropical anæmias, amœbic dysentery, sprue and schistosomiasis.

The work of the blood transfusion section of the pathology service in India deserves some special mention. It is hard to appreciate the energy and organization which made it possible for blood drawn in Dehra Dun or Poona to be dropped in Burma seventy-two hours later, yet such was a usual occurrence. It was the proud boast of the blood transfusion officers in India that no wounded man in Burma was ever denied a transfusion on account of lack of blood.

At the end of 1947, the service, so far as the officers of the R.A.M.C. were concerned, came to an end. The plans made during the war years had come to fruition and other schemes for the betterment of the service had been approved and handed over to our successors in Pakistan and India.

As was stated in the introductory paragraph, the fifty years which have just passed, is a long period of time to cover in a survey of progress in military pathology. It has, therefore, only been possible to sketch in the more notable progress, even then with many omissions, without reference to the hundred and one advances in method and technique which have been developed in all branches of the subject during that long period of time. Many new problems confront the service but there is little reason to fear that they will be tackled and overcome as they were in the past.

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Advances in Military Pathology during the Past Fifty Years

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