of yellow fever vaccine and its injection under standardized conditions, and to approve institutes for the testing of yellow fever vaccines; (4) to control the issue of yellow fever immunization certificates.

So far as the sanitary control of aerodromes and aerodrome areas is concerned, this implies something more than the biannual meeting of government officials which before the war occurred at the Office International d'Hygiène Publique in Paris. It would involve a partial abrogation of sovereignty on the part of the territories concerned, since the sanitary staff engaged in this work would be responsible not to local directors of medical services but directly to the World Health Organization of the United Nations.

In the age of the internal combustion engine the spread of disease can be held in check only by a scheme which is internationally sponsored and internationally controlled.

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ABACTERIAL PYURIA

WITH SPECIAL REFERENCE TO INFECTION BY SPIROCHAETES

BY

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AND

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The problem of sterile, amicrobic, or abacterial pyuria is occasionally brought up in medical publications in relation to a new case observed. It is a problem that has interested us for several years, and we have published some papers on the subject in Chilean medical journals (Vargas-Zalazar, 1937; Coutts, 1938; Coutts and Vargas-Zalazar, 1945); our findings, however, may not be generally known. In our opinion "abacterial" is the right designation for this syndrome, which may originate through ascending or descending infection of the urinary tract by viruses, spirochaetes, or protozoa. In most cases causative diagnosis was not made because dark-ground observation of centrifuged urinary deposit of bladder or kidney urine samples has not been incorporated into routine laboratory practice.

We refer later to cases of abacterial pyuria, which according to our findings are produced by spirochaetes. Our first suspicion of the possible action that some of these micro-organisms might have in the production of such a type of pyuria was aroused more than ten years ago.

A medical student consulted us for slight dysuria and cloudy urine, in the absence of urethral discharge, which had been troubling him for a few days. Prof. Bisquertt-Torres, who had charge of the case, found pus cells but no bacteria of any kind in urine obtained direct from the bladder. Cystoscopy revealed only a slight congestion of the trigone. Bilateral kidney-pelvis catheterization performed on two occasions showed numerous pus cells but no bacteria. Cultures and animal inoculations of urine from both kidneys and bladder failed to reveal Koch's bacilli. At the time Bisquertt-Torres and one of us (Coutts) thought that the most probable diagnosis was that of bilateral renal tuberculosis. Before travelling to Switzerland the patient visited his dentist, who removed a gold-filled molar which was somewhat tender on pressure and showed a certain amount of apical damage in a radiograph. Urinary symptoms then sub-

sided rapidly, the urine cleared, and the pus disappeared. He is now a well-known physician, is married, has several children, and enjoys good health.

In 1937 Vargas-Zalazar, at one of the weekly staff meetings of our clinic, presented a case of abacterial pyuria. In the discussion Coutts, remembering the above case and some similar ones presented by Wildbolz at the French Congress of Urology in 1933 and treated successfully with arsenicals, suggested a search for spirochaetes in urinary deposits observed under dark-ground illumination. These micro-organisms might proceed from the oral cavity or intestinal tract. In this case spirochaetes were discovered. On perusing the medical literature we found that Briggs (1935), Cook (1936), and Wildbolz (1937) had treated similar cases of abacterial pyuria successfully with arsenicals.

The following is a summary of five cases of abacterial pyuria in which we were able to demonstrate spirochaetes or spirilla under dark-ground illumination of deposit from centrifuged bladder urine obtained by catheter.

Case Reports

Case 1.—A male student aged 21 consulted Vargas-Zalazar privately in 1937. He had undergone tonsillectomy at 8 years of age. His present illness began in 1934, when, after gonorrhoea complicated by epididymitis, his urine on complete bacteriological recovery remained cloudy and contained pus cells. The attending urologist studied the case from a renal point of view and found abacterial pyuria in both kidneys. Investigations for Koch's bacilli were all negative. As the patient felt no symptoms he abandoned further medical care. In 1937 renewed urological studies by Vargas-Zalazar gave similar results. An intravenous pyelogram revealed a right hydro-uretero-nephrosis. Dark-ground investigation of bladder urine showed the presence of large numbers of spirilla. He was treated with one dose of 0.15 g. and three of 0.3 g. of neosalvarsan, and in twenty days pyuria and spirilla disappeared from the urine. Later controls have proved his cure to be complete (Vargas-Zalazar, 1937).

Case 2.—A merchant aged 47 consulted Coutts in 1937 because for two months a slight urinary diurnal frequency and tenesmus had been troubling him. His urine was cloudy and did not clear, nor did symptoms disappear after two successive courses of protosil album. On examination there was no urethral discharge, the urine was cloudy, and the prostate and genitalia were normal. Bladder urine contained numerous leucocytes and some red cells but no bacteria. Koch's bacilli were not seen. The bladder capacity was 150 ml., and the ureteral orifices were normal. On the trigone and right wall several aphthoid lesions were observed. Dark-ground illumination of the bladder urine deposit revealed numerous spirilla. Methylene-blue instillations into the bladder and three injections of a pentavalent arsenical intravenously cured him. When last seen he was in perfect health and his former trouble had not recurred (Coutts and Vargas-Zalazar, 1945).

Case 3.—A woman aged 34 entered our clinic in 1938. Her previous history was of no importance. The present illness began fourteen months before with slowly increasing urinary frequency by day and night. Terminal haematuria was occasionally present. The bladder urine contained pus and cocci, but Koch's bacillus was absent from several samples. The bladder capacity was 40 ml.; there was intense congestion of mucosa with numerous disseminated ecchymotic spots and patches, some covered by exudate. Local treatment was unsuccessful. Dark-ground examination of bladder urine deposit showed numerous spirilla. Arsenic and bismuth combined cured the condition rapidly (Bisquertt-Torres, 1938).

Case 4.—A married hospital nurse aged 32 began in 1940 to have painless haematuria lasting for two days. There was a similar recurrence in December, 1941. As the loss of blood was not stopped by treatment she was admitted to our clinic. Her bladder urine always showed red cells and a few pus cells but no germs. Koch's bacilli were never found. Blood pressure and coagulation tests were normal. Bilateral renal catheterization on two occasions showed blood in both kidney pelvis and very slight pyuria but no bacilli. Koch's bacilli were not found. A descending pyelogram proved normal. Dark-ground examination was positive for spirilla (bladder urine). She was treated with pentavalent arsenic by mouth, and haematuria then disappeared. In November, 1944, haematuria reappeared, and spirilla were found in bladder urine. She was cured with stovarsol and was sent to her dentist (Coutts and Vargas-Zalazar, 1945). Up to the time of writing she had relapsed once again.

Case 5.—A physician aged 49 consulted Coutts in 1946 for dysuria and cloudy urine. Five days previously a dead nerve was removed from the canal of an upper median incisor. A few hours later the upper lip started swelling, and twenty-four hours later an abscess of the anterior portion of the gum was drained surgically. Bladder

symptoms started shortly afterwards. There was no urethral discharge; pus was present in the urine, but no bacteria. Under dark-ground illumination a few spirilla were found. He had been taking sulphonamides. Stovarsol was given by mouth; bladder symptoms subsided and pus disappeared from urine.

Discussion

Cases of abacterial pyuria, besides those already quoted, have also been studied by Schaffhauser (1937), Houtappel (1939), Moore (1940, 1943), Cook (1944), Donovan (1945), Peters (1946), etc. Most of them have been cured with arsenicals, but in no case have spirochaetes been proved to be their cause, although they have often been considered as the possible aetiological agent. Peters (1946) brings this problem up again; because of the prompt therapeutic action of neoarsphenamine he believes that the causative organism belongs to the spirochaete group. The spirochaete, he thinks, has escaped identification, probably because of some morphological peculiarity. Except those published by us (Vargas-Zalazar, 1937; Coutts, 1938; Coutts and Vargas-Zalazar, 1945) only one case of pyuria by spirochaetes appears in the medical literature; it was also studied at the clinic here and reported on by Bisquertt-Torres (1938). According to our observations bladder and kidneys may become infected by the ascending or the descending route. Spirochaetal (non-syphilitic) infection of the male and female urethra is not uncommon. Descending infection is usually of the blood-stream type. Spirochaetes have been found in bladder urine in cases of so-called war nephritis (Salomon and Neveu), in trench fever (Nankivell and Sundell), in relapsing fever (Chung), and in Weil's disease. In our opinion the spirochaetes present in our cases might have a buccal or intestinal origin. Pettit (1928) considered the possible buccal nature of spirochaetes discovered by Croveri in stools; Buttiaux (1930) found them in stools of patients suffering from colitis; Doenges (1938) found them in gastric glands in 45% of 103 samples of stomachs selected from 3,400 necropsies; Kritchewski and Séguin (1923) found them in cases of retrograde pulpitis; Cavalé and Mandoul (1921) in alveolo-dental expulsive polyarthritides; Gins (1942) in cases of periodontitis; Saenz de la Calzada (1934) describes a case of urinary frequency of dental origin; Ferreira (1939) reports a case of metastatic infection of the prostate from a dental focus; Goldberg (1943) describes prostatitis and arthritis of dental origin.

In all our cases we found spirilla of diverse morphology; some were slender and had only a few spirals, while others were very similar to *Sp. dentium*. We believe they belonged to the buccal flora, but we have no further evidence of this. Treatment with pentavalent arsenicals was always successful. All cases were submitted to dental attention. In order to demonstrate the presence of these fragile micro-organisms we recommend slow and prolonged centrifugation of freshly obtained bladder urine. Before examining the deposit under dark-ground illumination it is advisable to add a drop of normal saline at 37° C. in order to increase the movements of the parasites.

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Ascorbic acid preparations may now be supplied to the welfare departments of factories. The Directorate of Medical Supplies of the Ministry of Supply, Portland House, Tothill Street, London, S.W.1, has taken over the supply and distribution of these preparations.

PERIPHERAL NERVE INJURIES

RECENT PROGRESS IN TREATMENT

BY

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The importance of peripheral nerve injuries in modern warfare is shown by the fact that Spurling and Woodhall (1946) estimate that there were 25,000 peripheral nerve injuries in the second world war, and that they formed 10.5% of battle casualties. There are no fewer than 7,000 end-to-end sutures in the U.S. Registry of Peripheral Nerve Injuries, which was established in November, 1944, to follow up these injuries and assess at regular intervals the results of treatment.

While the final results will not be available for some years, the preliminary reports of surgeons in both American and British neurosurgical teams and centres are of great value and convey information which must influence the future treatment of this type of injury. The opinion expressed in the *Report on Peripheral Nerve Injuries* which was published after the first world war (1920), that the results of treatment are largely independent of the interval between wounding and surgical repair, had already been disproved, as regards delayed suture, by the poor quality of the clinical results and the underlying reasons for failure explained by the important experimental work carried out during the last few years. Thus Holmes and Young (1942), Sanders (1942), and other workers showed that the poor results after delayed secondary suture were due to shrinkage of the neurilemma tubes in the peripheral segment, which delayed maturation of the down-growing axonal fibres; and Gutmann and Young (1944) found that with delay there is progressive atrophy in the muscle fibres and end-plates, so that the new fibres returning down the tubes are, after some months, unable to re-enter the old nerve plates. The resulting pattern of innervation is then far from normal, and many muscle fibres never recover at all.

It was therefore fully realized that delay in suturing was certain to lead to reduced efficiency of regeneration, but there was no unanimity concerning the respective advantages of primary and early secondary suture. The obvious arguments in favour of some delay in suture were: (1) to give time for at least some absorption to take place of the degeneration products in the neurilemma tubes in the peripheral segment and at the site of division; (2) Tello and Cajal's view that the new fibres are drawn into the peripheral stump by chemical attraction set up by the degenerated products, which reached its height two to three weeks after division of the nerve; (3) the possibility that the Schwann cells which line the walls of the neurilemma tubes regenerate rapidly after division and aid down-growth of the axonal protoplasm.

Cajal's views were adopted by Duel and Ballance (1932) with considerable success in experimental work on monkeys and in human beings, in whom Duel used degenerated autografts to repair defects in the facial nerve. These problems were, however, reinvestigated by Bentley and Hill (1936), who failed to find any evidence in favour of Tello and Cajal's theories, and their views are supported by Sanders and Young (1942). Abercrombie and Johnson (1942) and Young (1942) do not agree with these adverse findings regarding the advantages of predegeneration, and their conclusions accord more closely with the clinical results, about which there can be no dispute. These authors found evidence that degeneration of the nerve fibres caused activation of the Schwann cells, which reached its peak between the 19th and 25th days after section; and, since Schwann cells probably play an important part in forming the junction when severed nerves are repaired, they will be more active in joining together two nerve stumps if the nerve suture or nerve graft is left a few (say 10 to 20) days to degenerate before making the repair. "In this way there would be less likelihood that the Schwann cell junction will be hindered by the prior development in the suture line of serious fibrosis. The same argument indicates the use of predegenerated grafts, providing predegeneration is short (10 to 20 days)."

Advantages of Early Secondary Suture

The clinical results furnish strong evidence in favour of early secondary as opposed to primary suture. Zachary and