Abnormal Behaviour of *L. canicola*

At this stage in the investigation a paper by Das Gupta (1942) appeared in which he stated that a particular strain of *L. canicola* had recently become agglutinable by normal human serum. Das Gupta found that this non-specific agglutination did not take place if the serum were heated to 56° C. for half an hour before use.

This abnormality differs from the one we have described because the suspensions of *L. canicola* were agglutinated by normal serum. However, we retested several samples of the sera under investigation against the Jackson strain after they had been heated. The agglutination titres were reduced but not abolished. This reduction of titre is not due to destruction of complement, because sera which had been held at room temperature for periods up to six weeks still produced agglutination, and after that time no complement could have been present.

Reversion of *L. icterohaemorrhagiae* to Normal

The leptospira suspensions with which these investigations were carried out were prepared from serial subcultures of the strain, and the aberrant agglutinations occurred with the different lots in use from Sept. to Nov., 1942. Later in November it was realized that no further sera which were without effect on the other strains were agglutinating the Jackson strain. Samples of four sera which previously agglutinated the strain were still available and were retested. Now they also produced no agglutination. Since that time some 50 additional sera have been tested, but no further cases of non-specific agglutination have occurred. The suspensions, however, are still agglutinable to full titre when tested against immune rabbit serum.

Discussion

The agglutination of one strain of *L. icterohaemorrhagiae* by a number of sera which were negative with other strains, and the abrupt cessation of the phenomenon, seem to point to some temporary instability of this strain. It is of course well known that the agglutinability of strains varies greatly, and this strain was chosen because it agglutinated well. The medium used for culturing leptospira contains rabbit serum, and it sometimes happens that the serum of certain rabbits appears to retard rather than enhance the growth. Also, some apparently satisfactory cultures fail to agglutinate with specific antiserum. It might be argued, therefore, that some abnormality of the medium had produced unduly sensitive suspensions, whereas later subcultures in normal medium had reverted to their usual stability.

On the other hand there is the undoubted fact that the serum from only a proportion of cases of infective hepatitis gave positive results with these suspensions, and this seems to suggest that the sera possessed some unusual constituent which reacted with an abnormally unstable suspension.

Summary and Conclusions

More than 70 cases of jaundice occurring during the autumn of 1942 have been investigated. Of these, the sera of 34 agglutinated the strain of *L. icterohaemorrhagiae* (Jackson) that had been in use for eight years as a diagnostic antigen.

These "positive" sera failed to produce adhesion with the same strain, failed to agglutinate other strains of *L. icterohaemorrhagiae*, and failed to protect guinea-pigs against infection with a virulent culture of leptospira.

No leptospira were seen in the deposits of the centrifuged urine of these cases. Scarification of the deposits and inoculation of blood into guinea-pigs failed to produce infection.

Differential blood counts done on these patients were either normal or showed a relative mononuclear increase instead of the polymorphonuclear leucocytosis characteristic of Weil's disease.

The non-specific agglutinations are different from the false positives we have previously described. In our opinion they are due to an acquired abnormal susceptibility of the strain used as the antigen.

This instability was lost on further subculture, and the strain has apparently reverted to normal.

There must have been some additional factor present in the serum, because the sera of only a proportion of cases of jaundice produced this agglutination. Such an occurrence makes it necessary to employ cultures of more than one strain for diagnostic purposes.

We feel that this is an additional argument in favour of the view we have previously expressed that "until some method of standardizing cultures of leptospira is employed, the serological diagnosis of Weil's disease should be undertaken only at laboratories where the idiosyncrasies of the antigens are well known."

We wish to express our thanks to Col. W. H. O'Riordan, M.C., O.C. Cambridge Hospital, Aldershot, and to Lieut.-Col. N. T. Whitehead, M.C., R.A.M.C., assistant director of pathology, South-Eastern Command, for placing every facility at our disposal during this investigation.

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SYMPTOMATOLOGY OF MALARIA

BY

P. H. BIRKS, M.R.C.S., L.R.C.P.

Captain, R.A.M.C.

Since April, 1942, I have been medical officer to a unit heavily exposed to malaria. During the hot months we had many cases of acute febrile malaria, 80% of which were malignant tertian infections. Hyperpyrexial, cerebral, and bilious forms were encountered, and one quickly grew accustomed to the vagaries and complications of malaria in its acute forms, and later to the so-called chronic malaria with its enlarged spleen, anaemia, and general ill-health.

With the onset of the cold weather fresh cases rapidly diminished, although I was faced with a large number of patients with relatively trivial complaints whom I at first treated on conservative orthodox lines according to their symptoms, but with no success. Headaches and pains in the back were evidently not English aches and pains. Dismissing the possibility of malingering by reason of my personal knowledge of the patients, I remembered that the largest pathological factor in this part of India was malaria, and, having access to a microscope, I began a general investigation of all cases reporting sick.

I hope, by recording the following cases, to show that malaria is something more than an acute febrile disease, and that it can produce such varied symptoms as pains in the back, rheumatic pains about joints, pains in the testicles, urticaria, multiple conjunctival ecchymosis, cardiac irregularity, recurrent diarrhoea, and obstinate eczematoid conditions without fever. I cannot say dogmatically that these symptoms and malaria are direct cause and effect, but I suggest that there is weighty evidence in favour of this, having regard to the positive blood examinations and the results of treatment.

Case Records

Case 1.—Complained of severe pain in the back, worse at rest than when walking about; no history of malaria; treated for several days as lumbago with liniment and mist. sod. sal. without improvement. A thick blood film showed B.T. rings and trophozoites; the spleen was not palpable though the splenic area was dull to percussion. A standard course was given and all symptoms disappeared on the third day of treatment.

Case 2.—He had severe pain over second costal cartilage on left side. This appeared swollen and was tender on pressure. There was also clinical evidence of anaemia and general ill-health. A thick blood film revealed M.T. rings; the spleen was not palpable. After a course of standard treatment all symptoms disappeared.

Case 3.—This patient had severe pain in left side of chest over fifth, sixth, and seventh ribs, worse on breathing. There was no fever and no physical sign in the chest. The tip of the spleen was palpable, and a thick film revealed M.T. rings and crescents. All symptoms subsided after a standard course.

Case 4.—Complained of recurrent swellings of the face; there was no history of any previous allergic phenomena. A blood slide revealed B.T. rings and trophozoites. After a standard course no further swellings occurred. A previous similar case had been seen in a patient with recurrent benign tertian malaria. This man had urticarial swellings of face and over both tibiae and above the ankle-joint. A third case showing B.T. rings has also been seen.

Case 5.—He developed a patch of dry scaly eczema with occasional formation of vesicles and pustules just above the left knee; other less-marked but recurring areas of dry scaling with erythema were apparent on the flexor aspects of the arms. Exposure to sun aggravated the condition. The spleen was not palpable, but thick

blood film showed M.T. rings and crescents. There was evidence of anaemia. After a standard course the patches of eczema subsided for the first time over a period of three months.

Case 6.—He had clinical malaria four months previously and showed a large conjunctival ecchymosis. B.T. rings and trophozoites were found in thick film. No fever was present. Acute conjunctivitis with enlarged superficial blood vessels has also been seen which failed to respond to treatment on orthodox lines. M.T. parasites were found in thick blood film. The condition cleared after standard treatment. A third similar case of this type cleared very slowly under silver nitrate drops. Later, B.T. rings were found in the peripheral blood.

Case 7.—Complained of palpitation, and on examination a gross irregularity of pulse was found with dropped beats corresponding to extrasystoles, heard on auscultation of the heart. The irregularity disappeared on exercise. Thick blood film showed B.T. rings. After rest and standard treatment no further irregularity was detected. The spleen was not palpable.

Case 8.—Had pain in the left shoulder, slight pain in the right shoulder and left hip. There was low fever, 99° to 100°; the pulse rate was 120 standing and 90 lying. An apical systolic murmur was heard. A diagnosis of rheumatic fever was made, but a thick blood film showed M.T. rings. After a standard course he was restored to normal health.

Case 9.—Complained of pain and swelling in testicle. Right testicle swollen and acutely tender on palpation. Low fever 99° to 100°, headache, and malaise. A blood slide revealed M.T. rings and crescents. A standard course was given and the symptoms subsided rapidly. On rectal examination prostate normal; prostatic massage yielded only a little clear fluid; vesicles not palpable.

Case 10.—This is one case of many which showed identical symptoms—i.e., profound lassitude, frontal headache, and loss of appetite. No previous history of malaria. Thick blood film showed M.T. rings and crescents. There was evidence of anaemia. A standard course restored him to normal health.

Case 11.—Another example of several similar cases. Acute diarrhoea responding to intestinal sedatives but relapsing immediately these were withdrawn. There was loss of weight and appetite. Examination of the stools produced no microscopical evidence of disease. A thick blood film showed M.T. rings, and the diarrhoea responded to standard treatment.

Discussion

These cases suggest that the malarial parasite can exist in the peripheral blood and produce diverse pathological conditions without pyrexia.

The efficacy of treating a whole unit with antimalarial drugs—e.g., blanket treating—has been known for a long time, but with a supply of drugs that is not unlimited this is wasteful. Instead of indiscriminate "blanketing" it would be better to treat selectively, choosing any man obviously below normal health, where possible checking each case by thick blood preparations. It is a shibboleth that parasites cannot be found except in febrile cases. M.T. rings and B.T. trophozoites and rings can be found if the same diligence is used in searching a thick film as is necessary in thin films. The crescent, too, can be seen, though it is often too distorted for confident diagnosis.

Manson-Bahr describes a physical sign which I have found most useful as confirmatory evidence of malaria. In health the conjunctival blood vessels are few in number, pale-coloured, and of fine calibre; in other acute fevers they are often multiple and arranged radially, giving the eye a hazy pink appearance. In malarial infections, acute or afebrile, vessels of deep red colour and greater width can be seen winding a tortuous course on the surface of the conjunctiva. They are not especially numerous, nor is the whole of the conjunctiva necessarily involved. I have seen an extensive ecchymosis spread from one of these vessels during acute febrile malaria. If this can happen here it is probable that it can happen on any mucous membrane or indeed in any part of the body, and it offers an explanation of many of the obscure symptoms that may be encountered, such as the common throbbing frontal headache.

I submit that our conception of malaria as an acute fever is only one half of the truth and that it is also a generalized disease of arterioles and capillaries capable of producing a multitude of symptoms relative to the state and site of these vessels without any accompanying fever.

My acknowledgments are due to Brigadier McLeevey, who kindly read and approved this paper for publication.

GAS INFECTION OF THE BRAIN AS ONE FORM OF THE SERIOUS COMPLICATIONS OF CEREBRO-CRANIAL INJURIES

REPORT BY A COMMITTEE OF SOVIET SCIENTISTS (162)*

It is sometimes difficult to explain the various forms of serious complications arising from cerebro-cranial injuries. Very often these injuries run a different course in respect of the onset of granulation, conclusion of healing, and types of complications, in spite of the fact that they have the same localization, the force damaging the cranium is the same, and the missile is similar. The whole series of acute meningo-encephalitic complications which occur in the first stage of evacuation, in the F.M.H. (Field Mobile Hospital) of the first and second lines, attract attention and demand explanation.

It is now generally accepted that injuries sustained in the present war, including cerebro-cranial ones, are mostly infected. The range of pathogenic organisms infecting the wounds is very large. Gunshot and explosive missiles are in the majority of cases causing badly lacerated, contaminated, and consequently infected wounds. Data collected by Soviet authors and published during the civil war proved that the majority of cerebro-cranial injuries were caused by shell fragments, mines, etc.—not bullets—resulting in blind tracks, with retained pieces of clothing, dirty hairs, etc. Bullet wounds, particularly penetrating ones, were in the minority.

The Infective Organisms

We undertook investigations with the consent and support of the Chief Military Medical Directorate of the Red Army. We carried out intensive and detailed bacteriological examination of cases of cerebro-cranial injuries, and came to the conclusion that they were infected with the same micro-organisms as muscular injuries. Sterile wounds were rare: from 300 cases only 2 were registered as sterile. Of cases of cerebro-cranial injuries 61.7% were infected with cocci (*Streptococcus anaerobius*, *Str. pyogenes longissimus*, *Str. pyogenes longus*, *Str. brevis*, *Staph. pyogenes aureus*, *Staph. pyogenes albus*, micrococcus, diplococcus, *Gaffky tetragena*, etc.).

Of our cases 20.5% were infected with putrefactive aerobes (*Bact. megatherium*, *Bact. mycoides*, *Bact. mesentericus*, *Bact. subtilis*, *Proteus vulgaris*, *Kurthia zenkeri*). 11.2% were caused by gas-producing anaerobic organisms, the great majority (94%) being *Cl. perfringens*; next came *Cl. oedematiens* (12.1%)—in only one case was there *Cl. oedematis maligni*. 6.2% were caused by putrefactive anaerobes—*Cl. sporogenes*, *Cl. putrificum*, *Cl. butyricum*, and *Cl. tetanomorphum*. *Cl. perfringens* is usually found in cerebro-cranial injuries in combination with putrefactive anaerobes, aerobes, and streptococci.

Table I gives comparative percentages of various organisms in cases treated in the F.M.H. during 1½ months after the injury; in cases transferred from other hospitals 1½ to 2 months after the injury and treated in the neurosurgical clinic of the Institute of Experimental Medicine; and cases treated in the Institute of Experimental Medicine 1 to 1½ months after the injury and receiving a course of sulphonamide therapy.

TABLE I.—Percentages of Various Organisms

	F.M.H.	Neurosurg. Clinic	Sulphonamide Therapy
Pathogenic anaerobes ..	13%	6%	9%
Putrefactive anaerobes ..	15.5%	18.3%	2.6%
Putrefactive aerobes ..	38%	50%	13.1%
Pathogenic streptococci ..	35%	41%	7.9%
Various cocci ..	75.52%	80%	94.7%

The figures in the table show that the more serious types of infection are met with during the first few days; later some of the patients die, and in some the pathogenic organisms disappear and are replaced by non-pathogenic ones (cocci). In neglected wounds the percentage of putrefactive organisms

* Translated by A. Fry, M.R.C.S.