

It is not yet clear how far one can stimulate agglutinin formation without exhausting the mechanism of production. It has been noticed that in typhoid-inoculated subjects infected with *B. paratyphosus B* there is most usually a marked stimulation of the typhoid-inoculation agglutinins. It would appear from experience of these infections in triple inoculated subjects who had at some previous period\* also received a typhoid vaccine that their response is much more often slighter in extent or entirely absent.

Experience of the test in diseases other than enteric has confirmed that of Ainley Walker,<sup>6</sup> who states: "The rises in enteric agglutinin titre in association with other febrile conditions very rarely amount to as much as 100 per cent., and are much more frequently either altogether absent or so small as to be practically negligible." Conradi<sup>7</sup> has stated that he has demonstrated changes in titre which would be considered diagnostic in miliary tuberculosis, dysentery, pneumonia, erysipelas, and Weil's disease. It is not clear what method he adopted in carrying out his investigations, but the examination in this laboratory by Dreyer's method of many cases of similar disease has failed to show any appreciable variation of agglutinins in triple inoculated subjects.

Earlier experience of standard agglutinable cultures in non-inoculated and typhoid-inoculated subjects has confirmed the experience of Glynn and Lowe<sup>8</sup> "that co-agglutination between paratyphoid A and B, or vice versa, did not occur with the Oxford emulsions." Their opinion was based on a series of cases examined during convalescence. Examinations carried out during the active stage of the disease have made it clear that co-agglutination is not a factor which should cause difficulty in diagnosis.

I have to express my indebtedness to Lieutenant-Colonel C. R. Evans, D.S.O., R.A.M.C., who has kindly placed at my disposal the records of the cases referred to in this communication.

*Note by Colonel Sir WILLIAM LEISHMAN.*

Doubts have from time to time been expressed as to the diagnostic value of agglutination tests in fevers of the typhoid group contracted in men who had been inoculated with "T.A.B." vaccine. These doubts have frequently had special reference to the employment of Professor Dreyer's agglutination technique and of his standard emulsions, and to the validity of conclusions based on the behaviour of the agglutinin curves obtained with them. As this method is that which has been almost exclusively used in the B.E.F. in France, it has been suggested that our views as to its value ought to be put on record. To this end I accordingly asked Captain Perry, whose experience of this method is exceptionally wide, to undertake the above description of a series of his cases, which, it is hoped, will serve to demonstrate what we believe to be its great value. This opinion, I have reason to know, is shared by almost all the pathologists in France who have had occasion to employ it on a sufficiently large scale. Professor Dreyer may perhaps be a little too optimistic as to its simplicity and as to the facility of the interpretation of the agglutinin curves, but there can, I think, be no question but that a series of tests carried out during the attack, by experienced hands, is capable of giving clear indications as to the particular germ concerned in the infection in a large majority of the cases from which a bacillus cannot be isolated.

Captain Perry's article gives, as will be seen, only a series of illustrative cases, but these have been selected in such a way that they appear to cover most of the points which have been raised.

Careful records have been kept of the agglutination readings in the enormous majority of the cases of typhoid and paratyphoid fevers which have occurred during the operations in France, fortunately a very moderate number, which it is hoped may eventually be analysed. At present this is not possible, but it would be ungrateful to delay longer our acknowledgment of the debt we owe to Professor Dreyer's method, and also to the Medical Research Committee for the organisation and the regular supply to us of the standard emulsions and the necessary agglutination outfits.

*References.*—1. Ainley Walker: *THE LANCET*, Nov. 25th, 1916. 2. Directions for the Use of Standard Agglutinable Cultures, Department of Pathology, University of Oxford, on behalf of the Medical Research Committee. 3. Dreyer, G., and Inman, A. C.: *THE LANCET*, March 10th, 1917. 4. Dreyer, G.: *Proc. Roy. Soc. Med.*, 1915, vol. ix., Med. Sec., p. 9. 5. Martin, C. J., and Upjohn: *Brit. Med. Jour.*, Sept. 2nd, 1916. 6. Ainley Walker: *THE LANCET*, Nov. 25th, 1916. 7. Conradi and Bieling: *Deutsche med. Woch.*, Oct. 19th, 1916. 8. Glynn and Cronin Lowe: *Journal of the R.A.M.C.*, December, 1916; *THE LANCET*, 1916, ii., 222.

## SEPTIC PHLEBITIS DUE TO GUNSHOT WOUNDS.

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OFTEN to-day, in the treatment of gunshot wounds, we are confronted with a pyrexia for which no obvious cause can be found. In such a case it is well to consider the possibility of the presence of septic phlebitis.

In connexion with the frequency of septic phlebitis consequent upon gunshot wounds one cannot help being struck by the large percentage of cases in which evidence of broncho-pneumonia or pleurisy is found post mortem. Thus, K. Taylor<sup>1</sup> found pulmonary lesions in 42 out of 51 consecutive autopsies performed on men who had died from gunshot wounds.

To amplify the evidence obtainable from the post-mortem room I applied to Lieutenant T. H. G. Shore, R.A.M.C., who is in charge of the district mortuary, and he kindly undertook to look through the reports of the last hundred autopsies carried out in his department.

The results of Lieutenant Shore's inquiry showed that among 100 consecutive cases were 25 in which death had followed gunshot wounds of the limbs.

Location of wound.	No. of cases.	Phlebitis.	Broncho-pneumonia or infarcts.
Arm ... ..	3	0	2 (66·6%)
Leg ... ..	24	10 (41·6%)	9 (37·5%)

In two cases there were wounds of both arm and leg.

Pulmonary infarcts were found in four of the cases in which phlebitis was not observed, although the presence of the infarcts indicates that it was present.

The table bears out the main theme of this paper, that septic infection of veins is, so far as the base hospitals in France are concerned, the chief cause of mortality after gunshot wounds of the extremities.

### *Clinical Signs.*

The signs of septic phlebitis are not always so manifest as to be easily observed during life. They have to be sought with care, and even so may prove elusive and indefinite.

Of course, a red and tender track along the course of a superficial vein may lead to a ready diagnosis. But such an obvious indication is often lacking, although septic phlebitis is present; while in the case of a deeper vein there may be no visible or tangible evidence at all of thrombosis. Emphasis is needed on this point. A septic thrombus may be present in the common femoral vein, for example, without pain, tenderness on pressure, or any other local manifestation whatever. Even recognisable oedema, local or distal, may be absent.

### *Diagnosis.*

First of all is required a knowledge that the process does occur, and that local examination yet may fail to give a clue to its presence. Beyond this, weak though it sounds, we must rely upon surgical instinct to guide us aright.

A continued pyrexia for which we cannot otherwise account, especially if accompanied by rigors, always should lead us to suspect that septic phlebitis may be present. The development of broncho-pneumonia or pleurisy also should guide us into the same train of thought, and is occasionally the surest clinical evidence we can get; though by this time we shall have allowed the patient's jeopardy to get some way ahead of us.

In some cases there is a general diffuse oedema which is suggestive of phlebitis of a larger, deeply-seated vein. An amputation has been performed, the wound appears to be satisfactory, no local abscess can be detected, and yet the patient does not convalesce; pyrexia continues, and he seems to be going downhill. By comparison with the same part of the sound limb we find that the amputation stump is swollen. There may or may not be pitting of the skin on pressure; this is not so important, but the swelling is there, and strongly suggests the presence of deep-seated phlebitis.

A similar clinical picture, it is true, will be shown occasionally by an abscess which is tracking along the deep fascial planes, but inasmuch as both conditions require investigation by the knife no great evil will come to pass if before operation we find ourselves unable to say which of the two conditions exists. Nor if we happen to find an abscess need we neglect to consider the state of the veins in its immediate neighbourhood.

### *Treatment.*

The proper treatment consists in tying the vein at some point above the level of the clot, dividing it below the ligature, and either removing a length of the vein with its infected contents or, if this be not possible, opening the vein freely to afford drainage.

No doubt in some cases it would be sufficient to dispense with the proximal ligature, merely opening and draining the vein lower down in the limb. But as we have no means of determining beforehand in any

<sup>1</sup> *Annals of Surgery*, November, 1915.

particular case whether the progression of sepsis has or has not outrun the accompanying thrombosis, and as we are desirous to avoid detachment, even of uninfected clot, it will be safer whenever possible to occlude the vein above the lesion at an early stage of the operation, and so prevent the carriage of septic emboli to the lungs.

This, however, is not always feasible, as the clot already may have extended too far by the time the condition is recognised, and ligation of the proximal half of the subclavian vein or of the iliac veins, for example, is accompanied by practical perils which probably outweigh the hypothetical advantages. In such cases it will be the wiser course to open the affected vein at as high a level as can be reached without great risk, and to rely on drainage to prevent further spread of the infective process in a proximal direction.

In one case in which the clot had spread into the external iliac vein, and in which a transperitoneal operation was performed in order to ligate the common iliac vein above the level of the clot, the patient died of acute peritonitis. Examination of the clot in the external iliac vein in this case showed the presence of streptococci. In this case the vein was divided between two ligatures, and the peritoneal infection probably originated from the interior of the vein.

A useful point to remember when proceeding to tie a septic vein is that there are certain points in the course of a vein where clotting is apt to be checked for a while.

These are the levels at which large tributaries enter the vein. Thus, in an infection of the superficial femoral vein thrombosis is apt to be checked for a while at the places of entry of the profunda vein, and the internal saphena vein, while higher up the confluence of the internal and external iliac veins is another halting place, and still further up the union of the two common iliac veins is another obstacle to the extension of clotting.

Another anatomical fact which sometimes may afford useful suggestion is that the main channel by which blood returns from the leg is the superficial femoral vein, while the profunda vein is the main return channel for the thigh. This may help us to make a correct guess as to the seat of thrombosis, and will, in some cases at any rate, put us on the right track at the commencement of an operative search.

In the event of a thrombosed vein being discovered at an operation we may think fit to dissect out and remove as much of the diseased structure as is readily accessible. In doing this, it would be an error to apply a ligature to the distal portion, for if we cannot remove the whole of the infected vein we must not prevent drainage of the portion that is left. Therefore the distal part of the vein should be left open and in some cases its drainage may be facilitated by bringing it up to the surface and fixing it to the edge of the skin wound.

A cardinal rule in the treatment of any wound is to immobilise the injured part. This rule clearly has an added force when septic phlebitis is present, for in these circumstances any movement may assist in causing the detachment of clot with consequent infection of the lungs. Especially is care required during the manipulations necessary in transporting the subject to the operation table and during the operation itself. With regard to the latter it is a good plan, as soon as the upper limit of the clot has been defined, to tie the vein above this level before any further step is undertaken.

#### Cases.

Space permits only of the following cases noted. The great importance of septic phlebitis was not suspected until detailed observation at the mortuary brought the matter to light. Since then we have to some extent succeeded not only in recognising the condition in cases in which it probably would have been overlooked a little while ago, but in adopting remedial measures before the patient's deterioration has gone too far. We believe that the mortality of gunshot wounds can be considerably reduced by the earlier recognition of septic phlebitis and its appropriate treatment.

CASE 6. (Under care of Major H. A. Moffat).—Wounded in right heel on 15/11/17. Explored at C.C.S.; no foreign body found. On arrival at base on 17th wound septic; foot inflamed and swollen. Operation; additional drainage provided. 30th: Has had high pyrexia; to-day complaint of pain in right axilla, where pleural friction can be heard. Induration along course of internal saphena vein.

Operation.—Pus found in saphena vein in calf of leg. Just above knee saphena vein was thrombosed, five inches higher up it was not thrombosed, and it was ligated and divided at this point. 2/12/17: Rib resection for drainage of right streptococcal empyema. 3/1/18: Steady, uncomplicated recovery.

CASE 7.—Multiple wounds, received 14/12/17. Left thigh amputated at C.C.S. on the 14th. 21st: Continued pyrexia without rigors. 31st: Internal saphenous vein felt to be thrombosed.

Operation.—Exposure and removal of 5 inches of internal saphenous vein which is thrombosed up to where it enters common femoral vein. Abscess in left loin opened and drained. After-history: Uninterrupted recovery.

CASE 8. (Under care of Major H. A. Moffat).—Multiple bomb wounds, received 4/1/18. One of less severe wounds is a gutter wound in region of left elbow, not involving bones or joint. 9th: Some tracking of pus in left forearm and arm from elbow wound, with pyrexia. Anaesthetic. Cephalic vein found to be thrombosed. Vein ligated above upper limit of clot, and a length of thrombosed vein excised and sent to pathologist, who reported presence of streptococci in intravenous clot. 11th: Pyrexia continues. Forearm swollen. Anaesthetic given. Lower part of cephalic vein found to contain pus for some distance down forearm; below level of pus vein thrombosed as far as wrist; entire vein dissected out. 21st: Abscess in right foot opened and drained. After-history: Uneventful recovery.

#### Conclusions.

The following propositions may be advanced: 1. That septic phlebitis is a common complication of gunshot wounds. 2. That spontaneous recovery may take place, especially if small veins alone are involved. 3. That septic

phlebitis is often difficult to recognise during life. 4. That if its presence be overlooked, fatal complications are likely to ensue. 5. That timely surgical interference is attended with a good measure of success.

Finally, I should like to thank the medical officers under whose care the patients have been for permitting me to make use of their cases. I am especially indebted to Lieutenant Shore for the trouble taken in post-mortem examinations, and for analysing the results and permitting me to publish the statistical table.

## CEREBRO-SPINAL FEVER:

### NOTES ON 92 CONSECUTIVE CASES.

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THE patients whose notes are here briefly summarised have all come from one area in the field, were all soldiers between 19 and 48 years of age, and only two have come from anyone unit. These two, although in the same battalion, were in different companies, and had not been in contact so far as they knew. The incidence of the illnesses is shown in the accompanying chart.

All were nursed under canvas and were kept until fit to bear a train journey to the base. The average day of the disease when admitted was the fourth. All were treated with Lister or Pasteur serum, given intrathecally only, except in one instance in which it was given intravenously as well; this patient died. Lister serum was given at first and when its supply ran short Pasteur serum was substituted, the remaining Lister being hoarded for the milder cases, those in which the patient seemed to have a reasonable chance. This was done because the Pasteur serum would not agglutinate any of the strains of meningococci met with, and for this reason the comparison of results is perhaps a little unfair to the Pasteur serum.

In all the cases but six the meningococcus was seen in the cerebro-spinal fluid and in most cases cultivated. In these six the cerebro-spinal fluid was turbid and contained many polymorphonuclear leucocytes, and one of the patients died with the usual post-mortem appearances in the meninges of cerebro-spinal fever. Three of the six were in the Lister series and three in the Pasteur.

Thirty-three cases were treated with Lister serum. Of this number 18 recovered and 15 died. Of the recoveries two were completely deaf when evacuated and one was completely deaf in one ear. In none of the others was there any sign of permanent disability. One of the deaths was from streptococcal septicæmia, on the fifth day, when the meningeal symptoms were no longer marked, set up apparently by an intravenous saline administered before admission.

Fifty-two cases were treated with Pasteur serum. Of this number 33 recovered and 19 died. None who recovered had any sign of permanent disability. Among the deaths was one who lived for 65 days, long after all meningeal symptoms and signs had disappeared, and developed general anasarca with albuminuria, and was found post mortem to have large white kidneys. Two others died after meningeal symptoms had disappeared, of cystitis and pyelitis, set up, no doubt, by the catheterisation which had been repeatedly necessary in the early days of the illness. There was nothing macroscopically abnormal in the brains of these three.

Seven cases were treated with Lister and Pasteur serums combined. Of this number 3 recovered and 4 died. Of these patients, 4 began with Lister and were given Pasteur afterwards, rather as a forlorn hope, and all died; the other 3 began with Pasteur and afterwards had Lister owing to a temporary shortage of supply, and all recovered.

#### Symptoms and Signs.

Of the 54 who recovered, 21 were unconscious or delirious on admission and 33 sensible. Of the 38 who died, 23 were unconscious or delirious and 15 sensible. In every case the neck was definitely stiff, and in every patient who was not comatose or moribund on admission Kernig's sign was present at some time or other in the course of the illness. Twelve had rashes, 6 of these recovering and 6 dying. Twenty-two had one or more cranial nerves affected, strabismus being definitely noted in 16. Nystagmus has been quite common.