Editorial.

GAS GANGRENE.

At the outbreak of the Great War, 1914–18, gas gangrene was known as a somewhat rare complication of civilian surgical wounds, with an uncertain ætiology. The experiences of the South African War did not lead military surgeons to foresee the possibility of a large number of cases. In the early fighting around Mons and in the subsequent retreat there were not many cases, probably on account of the fine weather, open warfare, and the fact that many of the severely wounded were not evacuated. It was not regarded as a serious complication until the advance to the Marne and the fighting on the Aisne allowed of a greater proportion of wounded being observed. At this time there were more cases than at any subsequent period, and competent surgeons estimated that gas gangrene occurred in 10 to 12 per cent of the wounded. This was probably due to the number of wounded, slow evacuation, and want of knowledge of the danger of the condition, and the absence of surgical prophylaxis. In the middle of September, 1914, the Army Medical Service realized the importance of the condition and Professor Weinberg, of the Pasteur Institute, was asked to see some of the cases, and this led to his important work on pathogenic anaerobes.

Early in October the Army moved to Flanders, and immediately Sir Anthony Bowlby and Sydney Rowland investigated the condition. They eliminated the possibility of the disease being a hospital infection and it became important to ascertain and eliminate the predisposing causes.

The local condition of the soil appears to influence the incidence. In the South African War there was a hot dry climate and a sandy soil, and the disease was rare. On the Italian Front and on Gallipoli the disease was far less frequent than on the Western Front where the fighting was mainly on highly cultivated and fertile land.

Cases are more common in wet cold weather and it is the infiltration of the clothing that is of importance in this connexion.

The condition of the man when he receives his wound is of moment. Exhausted men are more likely to suffer from gas gangrene than troops who are fresh and well fed.

Deep wounds with much destruction of tissue and little or no opportunity for drainage are those most likely for gas gangrene to set in. Wounds in which the blood supply is interfered with in any way are favourable for the development of anaerobic bacteria. It is certain that the cutting off of the blood supply to a muscle is an important factor. Campbell and Pennefeather showed that some muscles, such as the gracilis, are dependent on a single main artery for their nourishment; others, especially the segmental muscles, have two or more arterial supplies. Their observations showed that the circulation within a muscle is largely a terminal one and that while the capillaries anastomose, the larger trunks do not. In the case of muscle with a single blood supply severance or thrombosis of the artery will render the muscle bloodless, but in the case of a muscle with several blood supplies the severance of an artery will not kill the entire muscle, but only its particular distribution. These facts explain how a dead or gangrenous muscle may be found in the midst of a healthy group and the arrest of disease at one point in a muscle. The subsequent death of a muscle apparently healthy at an operation may be due to the surgeon inadvertently interfering with the blood supply.

Gas gangrene can be most conveniently described under two heads: (*a*) Group gangrene, and (*b*) segmented gangrene (massive).

In group gangrene there may be a wounded muscle or muscle group from which the blood supply has been cut off, or infection of a muscle or group of muscles with an intact blood supply. In the first case a certain muscle or muscle group is dead but otherwise little altered except where wounded. Next to the dead muscle lies perfectly normal contractile muscle. The disease is, so to speak, a longitudinal one; infection finds difficulty in passing from one muscle to another, but easily extends up and down from end to end. The first change is in the appearance in the muscle involved: it has a salmon-red colour. This has been called the stage of "red death." About this time gas bubbles become evident to the eye and can be pressed up and down in the muscle tissue. The substance of the muscle becomes friable; the colour changes to yellow and possibly in the end the muscle becomes black and diffluent. The connective tissue near the muscle may be little altered; at other times it is filled with white or blood-stained œdema. Gas may or may not be present in the areolar tissue, and when present tends to find its way along the main vessels of the limb.

Infection of a wounded muscle or muscles with an intact blood supply is a comparatively rare phenomenon, living muscle shows a great resistance to invasion. When actual infection takes place the surface of the wound is dry or dirty looking, or in some cases black. Next to this is a red area which is limited towards the sound tissue by a yellow sinuous line. This line is raised and hard to the touch; next to it lies normal contractile muscle.

In segmental or massive gangrene all or nearly all the muscles of a segment of a limb distal to a complete arterial lesion, deprived of their blood supply, die and become infected.

Four organisms are mainly responsible for the disease: (1) *Bacillus welchii* (or *Clostridium welchii*).—This bacillus causes yellow œdema, large gas production of short duration, a salmon-red colour of the muscles, soft pulpy muscles, slight sourish smell, bronzing of the skin, appearance of fat globules in the discharge. (2) *Vibrion septique* (or *Clostridium œdematis maligni*).—This vibrion produces blood-stained œdema, large gas production, deep red colour of the affected muscle, an odour which is not putrid but rather rancid in character. (3) *Bacillus œdematiens* (or *Clostridium œdematiens*).—This bacillus causes colourless gelatinous œdema, a small amount of gas production, a pale pink colour of the muscles, deep red in heavily infected areas. (4) *Bacillus sporogenes.*—This bacillus produces an olive green colour of the muscles, the colour turning to black and a putrid odour. The bacillus is usually associated with *B. welchii* and may obscure the features of any of the gangrenous types. These organisms are all soprophytes and can only multiply in *dead* tissue. Some are sugar splitting and others proteolytic. They are spore-bearing anaerobes.

No precise information is available as to why the disease progresses in some cases and not in others ; why it returns after amputation, and why in certain cases treatment fails to arrest it. The advance in most cases is a local one, spreading centrifugally. A death of tissue is a necessary antecedent to the spread of bacteria. There is no difficulty in understanding the spread of infection in a muscle already deprived of its blood supply. The question is what kills the tissues when the blood supply is intact. Taylor advanced the view that the gas produces the death of the tissues by its disruptive effects, but it probably plays a secondary part by causing a tension which interferes with the blood supply. D'Este Emery has shown how the toxin repels the leucocytes ; indeed the absence of any reaction is one of the most striking phenomena often advanced of gangrene. None of the above facts affords an adequate explanation of the death of living tissue. The key to the problem lies in the observation that the bacteria washed free of toxin are comparatively harmless. Calcium salts have an important action in producing conditions suitable for the spores to germinate. Once this has occurred the organisms in the vegetative state elaborate a toxin which in untreated cases prepares the way for a further spread of the condition: (*a*) by killing the adjoining tissue and (*b*) by producing intense œdema which curtails the blood supply.

Certain areas of the body are noted to be the favourite sites for the occurrence of gas gangrene. The buttock is the commonest, then the calf and the hamstrings. The trunk is rarely affected and the disease never occurred on the scalp. The neck and erector spinæ are rarely affected.

The incubation period of gas gangrene may vary within wide limits. Definite gangrene with gas issuing from the wounds and œdema has been seen within five hours of the trauma, while on the other hand there are many recorded cases of gangrene having set in weeks or months after receipt of the original wound. These cases have often been associated with some operative procedure.

The starting point of gangrene is generally a wound infected by the passage of a missile with its accompanying layer of clothing or by particles of soil carried in with it. Damaged muscle, owing to the presence of glycogen, forms an ideal site for the development of anaerobic organisms. The production of œdema is the most striking characteristic of gas gangrene ; œdema always precedes gangrene and organisms may be detected in the fluid at levels at which no gangrenous change has taken place in the muscle. According to Wallace, pallor due to swelling of the deeper tissues is the first change noted in the skin ; this is succeeded by a dirty yellow discoloration followed by purple-red patches. The changes in the colour of the muscle are very constant. In the earliest stages the fibres are pale pink in colour, then the muscle looks puffy and dull in colour. The fibre is non-contractile and sinks in water. Later the fibre changes to green, brown, and finally black ; gas bubbles appear and the muscle has a honeycombed appearance and floats in water.

The bacteria proliferate freely in the wound and may be demonstrated in the tissues well in advance of the gangrenous process. In infections with *B. welchii* or *Vibrion septique* the number of organisms is enormous. In infections with *B. œdematiens* the number is trivial in comparison with the lesions produced. Blood infection is common in *Vibrion* infections, but in *B. welchii* infections it is usually terminal ; in *B. œdematiens* it is less common and also usually terminal. In reported cases of metastatic gangrene *B. welchii* is usually found.

The laboratory diagnosis of the types of bacteria present is difficult. The examination of films is of limited value. An indication of the infection may be obtained from the appearance of the fluid and muscles. *Vibrion septique* produces a definite red muscle, and rose-red œdema fluid ; *B. œdematiens* a white glairy fluid ; *B. welchii* a bronzing of the skin and brown or yellow discoloration of the muscles.

It is now generally recognized that two or more types of organisms are present in practically all cases of gas gangrene. For this reason multivalent serum is used. Attempts to use monovalent sera have been discontinued. For this reason the identification of organisms as a routine measure is not of practical importance.

The heavy mortality in gas gangrene is due, in part, to a late diagnosis. Early treatment can give a mortality as low as 5 to 15 per cent instead of the usual mortality of 40 to 80 per cent. E. Dunbar Newell points out the great value of roentgenograms in showing the presence of gas bubbles in the tissues, permitting a diagnosis to be made before the physical sign of crepitus. Rinehart was the first to call attention to the value of the roentgenogram in making a diagnosis before the infection is clinically apparent. In suspected cases the roentgenogram should be repeated every four hours. If there is a steady increase of gas bubbles in each succeeding film it may be concluded that they are not due to inclusion of air in the wound.

The surgical factor in the disease is of the greatest importance. When the wounds are opened, cleaned, and drained, there is a great decrease in the number of cases, but it was not until complete excision of the wound became a standard method of procedure that gangrene ceased to be a serious menace. Thus in 1918, in a series of 40,000 wounded from two army fronts, only 400 cases of gangrene were recorded. Towards the end of hostilities the cases in which gangrene occurred were those in which the patients were suffering from severe shock which precluded surgical interference, or those in which loss of blood from a severed vessel rendered the patient's resistance negligible.

As the war progressed delay in treatment was reduced to a minimum. The time factor when infection is established is considered to be of greater importance in gas gangrene than in any other disease.

It is now recognized that in the treatment of gas gangrene all devitalized tissue, especially muscle, must be excised, adequate drainage provided, and the part immobilized. Böhler relies entirely on these measures; he does not even use prophylactic serum, and in 1933 he could write they had never failed. Trueta saw only one case of gas gangrene develop in over 1,000 fractures treated by his methods in Barcelona during the Spanish War, whereas the condition was already present in several patients transferred to his clinic many hours after injury. As we reported in the Editorial on his methods, his experiences emphasize the need of making the interval between injury and operation one of minutes rather than hours. He advocated immediate removal of all cases to hospital and that no time should be spent in first-aid attentions. In the *Lancet* of November 4, 1939, Brittain describes a case in which expectant treatment proved successful. Mitchener and Cowell recommend injection of hydrogen peroxide into the surrounding tissues to prevent the spread of anaerobic infection.

While the treatment of gas gangrene is essentially surgical, there was some evidence, however, in the Great War that antitoxic sera might be of use, but it was not until 1918 that antitoxic sera were used by the British Army. In the winter of 1918 Major Bull, of the United States Army, brought from America a small stock of *B. welchii* antitoxin which was used in a few experimental cases on the British front, but it became evident that to obtain general success it would be necessary to use a serum which contained the antitoxins of other pathogenic anaerobes. In April, 1918, a serum was supplied by Messrs. Burroughs Wellcome which contained the antitoxin of *B. welchii* and of *Vibrion septique*; the titre was not high and the results were disappointing on the whole, but the results in some cases were so striking as to leave no doubt that they were due to serum treatment.

It was considered that the serum should be given early to all wounded men with gross injury of muscle, to all cases in which a large artery is severed, to all cases in such a state of shock that they must be allowed to resuscitate before an operation is possible. The serum should be polyvalent with the weight thrown on *B. welchii* antitoxin. In the case of established gangrene the serum should be given intravenously and in large doses. It should also be injected into the muscles around the focus and by installation into the gangrenous focus. The injections should be repeated every few hours intravenously, and locally at every dressing and operation.

In the summer of 1918 a considerable experiment on prophylaxis was attempted under the direction of Colonel S. L. Cummins. Antitoxin for *B. welchii* was introduced into the antitetanic serum, which was being used as a prophylactic for all wounded. The results showed that the number of cases occurring in the casualty clearing station were not influenced and the incidence at the base was probably diminished. The mortality in the base hospitals was reduced by 50 per cent. Wallace, reporting on this trial, gives the figures from May to September of the wounded who received the combined sera and those who received antitetanic sera only at advanced dressing stations and developed gas gangrene before evacuation from the casualty clearing stations. He considers this series gives the only reliable figures for the whole compaign. Gas gangrene occurred in a little over 1 per cent of all wounds. There was no appreciable difference in the incidence of the disease receiving the two types of serum.

The French Medical Service used an anti-*welchii*, anti-*Vibrion septique*, and an anti-*œdematiens* serum. The three sera were injected about the damaged muscle in cases in which it was thought gas gangrene was likely to occur. The French reports of this treatment were somewhat enthusiastic. Weinberg placed a more potent serum at the disposal of the French service and good results were obtained by Duval, Chutro and Delbet.

The German surgeons claimed that much benefit resulted in their armies from the use of a polyvalent serum.

Opinions still vary as to the use of antiserum; some workers report successful results from the use of large doses. There is evidence that it is of value in lengthening the incubation period and in lessening the severity of the attack.

Welch, *Vibrion septique* and *Œdematiens* antitoxin may be administered, either separately or combined. In addition, an injection of one or more of these antitoxins *combined with Tetanus antitoxin* may be given.

The dosage may have to be modified in the light of experience, but the present provisional proposal is as follows:—

Prophylaxis as a combined injection.

Welch	.. ..	3,000 units
Vibrion septique	..	1,500 ,,
Œdematiens	..	1,000 ,,

This is contained in a dose of approximately 10 cubic centimetres.

Treatment, 25 cubic centimetres of the above serum (or two and a half times the prophylactic dose) may be given for therapeutic purposes in established cases.

The injection of a polyvalent serum may be replaced by a monovalent serum in areas where experience suggests that this is warranted, or for intensive specific serum therapy in cases in which the causative organism has been identified.

Kelly and his co-workers are enthusiastic about X-ray treatment, and their results justify a trial of the method. There were 29 cases in which amputation was not performed and all the cases recovered. Out of 15 cases who had amputation five died.

Chemotherapy is recommended by Böhlman, who records the recovery of three cases of gas gangrene after treatment with sulphanilamide. Jansen and his colleagues have reduced the incidence of infection in compound fractures by putting crystalline sulphanilamide into the wound before suturing it. On the other hand Kendriek found sulphanilamide and related compounds quite unable to save guinea-pigs experimentally infected with *B. welchii*, but as there is some evidence in their favour, it is thought these compounds should be used in all established cases.