and to our young comrades who, in the capacity of liaison officers, have been responsible for contact and have had to bear the brunt of the "paper" war. We have enjoyed far more than ordinary loyalty and comradeship. All things possible have been done to smoothe the way for us. These friends, who were worn out by hard work and sorely tried by personal grief, have by sacrificing much-needed time for rest and recreation not only carried out our wishes but even tried to forestall them.

THE RATIONALE OF COMPLETE IMMOBILIZATION IN TREATMENT OF INFECTED WOUNDS

BY

J. TRUETA, M.D.

AND

J. M. BARNES, M.B., B.Ch.

(From the Nuffield Department of Orthopaedic Surgery, Oxford)

With the prospect of thousands of casualties arising in the near future from gunshot wounds and from bomb splinters it becomes a matter of urgency to review the methods at present advocated for their treatment. If one may judge from articles in recent numbers of our medical journals it would appear that surgeons with extensive experience of the treatment of injuries during the last war are still recommending those methods which they considered most satisfactory in 1918. Some reference may be found to the fact that a new method based on the work of Winnett-Orr has been employed by the surgeons of the Republican side during the Spanish Civil War.

It is the purpose of this review to summarize the available literature dealing with the spread of infection in the body, particularly in the limbs, and to show that a good case based on experimental work may be made out for the closed-plaster method of treating infected wounds. The essential feature of this method, which has been fully described by Trueta (1939a), is the complete immobilization of the soft tissues. The experience gained from its use in the treatment of large numbers of infected wounds has shown that under conditions of complete immobilization the tissues of the body are capable of resisting invasion by many different varieties of bacteria, even when the latter continue to grow freely in the wound. Later, when the initial danger of invasion has been overcome, the cells and body fluids are capable of destroying these organisms and allowing the normal processes of repair to take place.

From the outset it must be emphasized that the aim of this form of treatment is to provide the optimal conditions for the body itself to destroy the invaders, and no attempt is made to kill them by external agents: this consideration is paramount, irrespective of the possible virulence of the organisms that might be present. It is obvious that if the common pyogenic bacteria (but perhaps not organisms that normally remain fixed and damage the host by the production of a powerful exotoxin) can be kept localized in the tissues their power to injure the host is very much diminished.

Experimental Evidence

Movement of Bacteria in the Body.—It has long been known that bacteria can travel very rapidly from recent wounds to the internal organs; indeed, non-pathogenic bacteria have been found in the spleen five minutes after being placed in wounds on the backs of rabbits (Schimmelbusch, 1894). This rapid spread must mean that organisms enter either the blood stream or the lymph stream. It is difficult to imagine them entering directly through the cut ends of the smaller vessels; either these would be blocked by thrombi or, if still patent, the current of the escaping fluid should prevent particles being carried in. The bacteria must penetrate the walls of the blood or lymph capillaries. Pawlowsky (1900) was convinced that bacteria travelled by the lymphatics. In support of this it has been found that bacteria injected into the knee-joints of rabbits may be isolated from the inguinal, iliac, and lumbar lymph glands within ten minutes of the injection. It also indicates that the glands do not invariably act as efficient filters for the organisms (Noetzel, 1906). Three varieties of bacteria injected under the skin on the backs of rabbits have been cultured from the lymph obtained from the thoracic duct at a time when cultures of the blood were sterile (Finucci, 1935). Wells and Johnstone (1907) showed that *B. coli* injected into the peritoneal cavity of dogs appeared in large numbers in the lymph from the thoracic duct; in rabbits they found that *B. coli* placed in the peritoneal cavity reached the blood stream after a longer interval, and in smaller numbers if the thoracic duct had been tied. Similarly, virulent bacteria placed in the nasal cavities of rabbits can be isolated from the lymph removed by a cannula from the cervical lymph duct (Schulz, Warren, and Drinker, 1938). The exact mechanism by which the bacteria reach the lymph is not clear. Although lymph draining an inflamed area may contain large numbers of polymorphonuclear leucocytes (Menkin, 1929), virulent capsulated bacteria that are not phagocytosed may readily enter the lymph stream (Field, Schaffer, Enders, and Drinker, 1937).

Absorption of Substances from the Tissues.—Absorption is carried out by both the blood and lymph streams; the amounts removed by each are dependent upon the size of the molecules of the substance being absorbed. Those of low molecular weight are absorbed by the blood stream alone; as the molecular weight rises so does an increasing proportion get carried away by the lymphatics (Drinker and Field, 1933). Substances of a molecular weight equal to that of serum proteins are absorbed entirely by the lymphatics. This has been shown to be the case both for subcutaneous tissues (Lewis, 1921) and for joints (Bauer, Short, and Bennett, 1933). Since this is the chief channel of absorption for protein particles of relatively small size it is not surprising to find that microscopically visible particulate matter travels entirely by the lymphatics and not by the blood stream. This, for instance, has been shown to be the case in studies on the absorption from joints (Bauer, Ropes, and Waine, 1940).

Importance of the Lymph Stream.—It is obvious that any measure that will reduce the amount of lymph flowing through a limb must at the same time greatly decrease the chances of absorption of bacteria and their toxic products. It is well known that the amount of lymph draining from a limb can be varied within very wide limits by relatively simple means. Thus it is impossible to obtain any lymph from the leg of an animal at rest; it begins to flow as soon as the limb is moved or massaged. Recent work has shown that both the amount of lymph produced and the rate at which it flows can be greatly increased by active or passive movements, by warmth, and by massage

(White, Field, and Drinker, 1933; McMaster, 1937). Furthermore, this increased lymphatic flow is associated with an increase in the speed of movement of particles and colloidal substances through the tissues (Florey, 1927; Allen, 1935; Bauer, Ropes, and Waine, 1940).

Application of this Knowledge

(a) *Freshly Inflicted Wounds.*—It is clear that in a limb completely immobilized the flow of lymph will be greatly slowed or perhaps completely arrested; as a result bacteria and their toxins will have reduced opportunities of reaching the general circulation. It also follows that immobilization should be instituted before the bacteria have had time to multiply, but must on no account be done before a thorough excision of the dead tissues has been carried out. The immobilization must be complete and include putting the muscles at rest. It is quite inadequate to immobilize the joint alone, for this will not prevent muscle spasm whenever the limb is disturbed, and muscular movements are most important in the production of a brisk lymph flow.

(b) *Wounds of Over 12 Hours' Duration.*—In wounds that have been present for twelve hours or more inflammatory changes will be present. It has been shown by many workers that if inflammatory changes are brought about in tissues by the injection of irritants bacteria when introduced tend to remain arrested at the site of injection and diffuse out either slowly or not at all. This has been shown to be the case in the peritoneum (Issaeff, 1893), in the knee-joint (Pawlowsky, 1909), and in the skin (Menkin, 1931). The mechanism of this so-called fixation is obscure; at all events it does not present an absolute barrier to the passage of substances through it. Field, Drinker, and White (1932) showed that dye was fixed in the inflamed paw of a dog and did not appear in the lymph flowing from the limb in spite of the fact that a great deal more lymph was being produced than from the undamaged limb. However, if the paw was moved or squeezed dye rapidly appeared in the lymph. This increased flow of lymph from an inflamed area means that should anything succeed in penetrating the fixation barrier it will stand a greater chance of being carried away. It follows that complete immobilization of an inflamed wound will reduce the chances of bacteria passing out of the inflamed area into the general circulation.

(c) *Healing Wounds.*—In still older wounds a layer of granulation tissue will be formed, and this is known to be impermeable to many different varieties of bacteria, including, for instance, streptococci (Halley, Chesney, and Dresel, 1927). But in order that this granulation tissue should be able to resist bacterial penetration it must present an unbroken surface. Everyone knows that the removal of dressings invariably abrades the raw area, and creates numerous tiny wounds each of which is capable of allowing the ingress of bacteria. By dressing the wound as infrequently as possible the granulation tissue is left undisturbed to act as a most effective barrier against invading bacteria. These conditions are satisfied when the closed-plaster technique is employed and the wound is left undisturbed for days or even weeks at a time. The validity of these contentions is borne out in practice by the following observations made in the course of the treatment of large numbers of cases during the Spanish Civil War.

1. Streptococcal septicaemia, which was the commonest cause of death among the wounded during the last war (Colebrook, 1939), was rarely observed in cases treated by this method. This is the more remarkable since in the majority of the cases streptococci could be grown from the discharges coming from the wounds.

2. Patients with extensive wounds invariably developed some pyrexia for a day or two after a change of plaster. This indicated that absorption of bacteria or of their toxins had resulted from the disturbance of the wound.

3. When the plaster was removed the granulation tissue always had a bright red healthy appearance, indicating that an active healing process was going on even in the presence of large numbers of bacteria.

Discussion

Hitherto in the treatment of infected wounds the efforts of surgeons have mainly been directed towards the use of antiseptics for the purpose of destroying bacteria. Far too little attention has been paid to the natural powers of the tissues to localize and kill bacteria.

In spite of an immense amount of work by chemists and bacteriologists there has yet to appear the ideal antiseptic for local application to the tissues that will destroy the bacteria and leave the tissues undamaged: even if this ideal antiseptic were found its application would result in frequent disturbances of the injured part.

The method of treating infected wounds in a closed plaster cast appears to offer a solution to the problem, and is based on entirely different principles. The essential features are a preliminary cleansing of the wound, preferably by soap and water, followed by a thorough excision of all dead tissues or of those whose survival seems doubtful; adequate drainage is ensured by opening up all the deeper tissues. There must be no opportunity left for the development of tension in the intermuscular spaces, the retention of discharges, and a consequently increased chance of absorption. It is absolutely essential that the surgical treatment should be thorough, and when the limb is finally enclosed in plaster this should be of sufficient extent to give complete immobilization to all the soft tissues. Under these conditions it is no longer necessary to worry about the growth of bacteria in these wounds, for the healthy tissue underneath presents an absolute barrier to their entry into the general circulation.

It seems probable that the secret of success in the use of this method lies in the complete immobilization of the injured and infected part. In all methods involving the continual use of antiseptics the wound is disturbed at intervals for the change of dressings. Even if the limb is supported on some open splint the pain caused by the manipulations will give rise to muscle spasm; also, the change of dressings damages the growing surface of the granulation tissue.

Conclusion

No new observations have been brought forward in this article, but an attempt has been made to explain the striking success of a relatively new method of treating infected wounds.

The methods described elsewhere (Trueta, 1939b) may not be perfect, but it is felt most strongly that improvement will only follow if the outlook of surgeons is fundamentally altered. Their aim should be to make sure they are giving the injured tissues the very best conditions to enable them to destroy the bacteria, and at the same time they should avoid damage to the cells by the application of antiseptics.

The perfect antiseptic may prove as elusive as the Philosopher's Stone, and until it is found it seems best to leave the task of destroying bacteria to the human body, which in the performance of its normal functions kills enormous numbers every day.

REFERENCES

Adkins, E. W. O., and Davies, D. V. (1940). *Quart. J. exp. Physiol.*, **30**, 147.
Allen, A. L. (1935). *S. Afr. J. med. Sci.*, **1**, 31.
Bauer, W., Short, C. L., and Bennett, G. A. (1933). *J. exp. Med.*, **57**, 419.
—— Ropes, M. W., and Waine, H. (1940). *Physiol. Rev.*, **20**, 272.
Colebrook, L. (1939). *Proc. roy. Soc. Med.*, **33**, 72.
Drinker, C. K., and Field, M. E. (1933). *Lymph and Lymphatic Tissue*, London.
Field, M. E., Drinker, C. K., and White, J. C. (1932). *J. exp. Med.*, **56**, 363.
—— Schaffer, M. F., Enders, J. F., and Drinker, C. K. (1937). Ibid., **65**, 468.
Finucci, V. (1935). *Pathologica*, **27**, 518.
Florey, H. (1927). *Brit. J. exp. Path.*, **8**, 479.
Halley, C. R. L., Chesney, A. M., and Dresel, I. (1927). *Johns Hopk. Hosp. Bull.*, **41**, 191.
Issaeff (1893). *Z. Hyg. Infektkr.*, **16**, 287.
Lewis, J. H. (1921). *J. Amer. med. Ass.*, **76**, 1342.
McMaster, P. D. (1937). *J. exp. Med.*, **65**, 347.
Menkin, V. (1929). *Arch. Path.*, **8**, 263.
—— (1931). *J. exp. Med.*, **53**, 647.
Noetzel, W. (1906). *Beitr. klin. Chir.*, **51**, 740.
Pawlowsky, A. D. (1900). *Z. Hyg. Infektkr.*, **33**, 261.
—— (1909). Ibid., **62**, 433.
Schimmelbusch, C. (1894). *Dtsch med. Wschr.*, **20**, 575.
Schulz, R. Z., Warren, M. F., and Drinker, C. K. (1938). *J. exp. Med.*, **68**, 251.
Trueta, J. (1939a). *The Treatment of War Wounds and Fractures*, London.
—— (1939b). *Proc. roy. Soc. Med.*, **33**, 65.
Wells, H. G., and Johnstone, O. P. (1907). *J. infect. Dis.*, **4**, 582.
White, J. C., Field, M. E., and Drinker, C. K. (1933). *Amer. J. Physiol.*, **103**, 34.

TRANSFUSION OF FRESH AND STORED BLOOD *

BY

H. F. BREWER, M.D.
N.E. London Blood Supply Depot

MONTAGUE MAIZELS, M.D., M.R.C.P.
S.E. London Blood Supply Depot

J. O. OLIVER, M.B., B.S.
S.W. London Blood Supply Depot

AND

JANET VAUGHAN, D.M., F.R.C.P.
N.W. London Blood Supply Depot

The object of the present investigation was to obtain information on: (1) the relative therapeutic value in cases of acute and non-acute haemorrhage of transfusions with fresh and stored blood; (2) the relative incidence and character of reactions following the use of fresh blood and stored blood.

Clinical Material used in the Investigation

Many clinicians in the hospitals in the four depot areas collaborated in this investigation by referring cases requiring blood transfusions to the clinical observers attached to the four depots. The general treatment, which was under the direction of the physician or surgeon in charge of the case, was not confined to blood transfusion. This meant that, in many instances, in addition to the transfusion of test material the patient was given saline, glucose saline, or iron and other therapy, which rather confused the picture. For our purpose cases have been divided into three groups:

(i) Acute haemorrhage (considerable blood loss within twenty-four hours of administration).

(ii) Non-acute haemorrhage (simple blood loss at least twenty-four hours before the transfusion or repeated haemorrhages over a long period).

(iii) Miscellaneous—which includes cases of haemorrhage complicated by gross sepsis, obscure anaemias, and patients subsequently found to have some complicating condition, such as leukaemia or malignant disease. Whether a patient were given fresh or stored blood depended on a number of factors. In a few cases the physician or surgeon in charge was insistent that fresh blood should be used. In some instances, analysed in detail, patients were given a transfusion of fresh blood followed after an interval by stored blood, or vice versa.

To obtain uniformity in the presentation of essential facts the clinical observers were asked to furnish particulars concerning each case transfused. The important points in the analysis of the information are presented in the tables which follow.

All blood used was obtained from the four depots. Two parts of blood were added to one part of diluent, consisting of 3% glucose in 0.85% sodium chloride and 1.05% sodium citrate. *Fresh blood* we defined as blood that had been stored for less than twenty-four hours; *stored blood* as blood that had been kept from ten to fourteen days. Blood was given by the Medical Research Council apparatus, except in a few instances when hospitals preferred to use their own.

Method of Examination

A. Clinical.—The difficulty of obtaining an objective measure of improvement or lack of improvement in a series of cases seen by different observers was appreciated from the outset. Improvements in pulse and blood pressure are a valuable indication in patients with shock and acute haemorrhage, but are less important with non-acute haemorrhage. An attempt has been made to assess various factors such as improvement in colour and general well-being and mental attitude under the term "general improvement."

B. Pathological: Red Cells and Haemoglobin.—A rise in the number of red cells and the haemoglobin level might be expected to offer a measure of satisfactory haematological response. Red cell counts and haemoglobin estimations were therefore made whenever possible. In the accompanying tables an increase in haemoglobin has been expressed not as an absolute figure but in relation to the amount of blood given. The observed gain has been divided by the number of bottles administered; the figures shown therefore represent the gain per bottle, each bottle containing 360 c.cm. of whole blood—approximately two-thirds of a pint. Haemoglobin was always estimated by Haldane's method. Before accepting the results it is important to realize there are possible difficulties in their interpretation.

Errors of the Method: 1. Colorimetric Error.—Any colorimetric method of estimation is open to error. In practice in one laboratory it has been found that technicians practised in using the Haldane standard will usually estimate any sample of blood within 2% of one another. It was felt that such sources of error were equally present in all cases. Therefore if a significant rise in haemoglobin was found in one group of cases and not in another it might be accepted as an indication of greater improvement in the former. Since haemoglobin usually runs parallel with the red cell counts and haematocrit readings in the type of cases under consideration the two latter have not been tabulated, though they were noted in making the analysis.

2. Normal Daily Variation.—Several observers have shown that in a normal person the haemoglobin may vary by as much as 8% in twenty-four hours: small individual variations are therefore probably without significance.

3. Blood-volume Changes.—In a patient with acute haemorrhage rapid changes in blood volume take place. There is no satisfactory method of estimating blood volume, especially in patients who are acutely ill. The influence of such changes on the circulating haemoglobin cannot therefore be estimated. An apparent fall in haemoglobin immediately following transfusion may be due only to blood dilution or to a persistence of bleeding. In acute cases haemoglobin estimations were therefore felt to be of little value between case and case, but probably were of some significance where two large groups, one receiving fresh blood and the other stored blood, were compared.

4. Raised Plasma Bilirubin.—Following the use of stored blood there may be a rise of plasma bilirubin in the first twenty-four

* Preliminary report on their relative values made for the Blood Transfusion Research Subcommittee and the Committee on Traumatic Shock of the Medical Research Council.