The nature of wounds produced during the present War has materially altered the views of surgeons, and made inadequate methods of treatment to which they have long been accustomed in civil practice. The ordinary technique of wound treatment fitted for civil hospitals has been found wanting in military surgery. We have grown so accustomed in virtue of the antiseptic and aseptic treatment of wounds, both before and after operation, to expect in a healthy wound healing without suppuration that when confronted with wounds already infected, as gunshot wounds are, we were unprepared to alter our methods of treatment to cope with such new conditions as have arisen.

The wounds caused during the present European campaign are very different to those which occurred during the South African War, and there appear to be two main points of difference:—

(1) The Environment.—The seat of War in South Africa, was a vast track of virgin soil, sparsely populated, uncultivated, except
in the neighbourhood of towns and rivers, and so particularly free from organisms. The climate, except during the rainy season, was exceptionally dry, the air was free from moisture and the soil over which our armies passed was sandy and mostly stony or rocky. The sun shone brilliantly all day and almost every day, and in such condition septic infection of wounds was the exception rather than the rule.

In Flanders and Belgium almost opposite circumstances prevail. The land has for generations been laid out for intensive cultivation and is therefore well farmed, it is thickly populated and enriched by manures—the excreta of men, horses, and cattle. Such a soil lends itself to the growth of very mixed and generous flora of organisms, and when one considers that it is in surroundings such as these that the trenches are dug, and in which our armies are living and fighting—their clothes and persons contaminated with a highly infected mud and soil, one ceases to wonder that the conditions of the wounds are so changed for the worse. Also the rainfall is great and the amount of sunshine comparatively small.

(2) The Nature of the Wounds. is also materially different to those seen in the South African War because the character and construction of the projectiles causing them are changed.

In the Boer War a bullet fired from a Mauser rifle was the chief cause of wounds. This bullet had a blunt rounded point of almost the same circumference as its base, and as it was usually fired at a considerable distance, the bullet had time to settle down in its flight and to get rid of the “wobbling,” which occurs in a bullet fired at less than 300 yards. The result was a clean cut hole both at the points of entrance and exit with little bruising of the tissues between. Even when a bone was struck it was generally pierced by a hole such as would be bored by a gimlet, and attended by little or no splintering. The present German bullet, in contrast to this is, more frequently than not, fired at close quarters either from rifle or machine gun, it is conical in shape with a sharp point so that the centre of balance is moved further back towards its base. The “wobble” therefore in this bullet is greater than in the one previously described, and it is more easily turned off the straight. Coming in contact with any resistance—soft tissues and more especially bone—the bullet is listed sideways, or in some cases makes a complete somersault, so that its base travels first and acts as a modified “Dum-dum.” It follows that though the wound of entry may be small like the “bug-bite” characteristic of the South African War, it is exceptional for the wound of exit to be a
small, clean-bored one. The characteristics of the exit wound are ragged edges and some tissue carried away. In addition the amount of tearing, bruising and concussion to intervening tissues is such that their resisting power is so lowered that they form a suitable nidus for the growth and development of organisms carried into the wound.

A still more important difference is due to the fact that the prevailing type of wound caused in this War, in contrast to that in South Africa, is produced by shells which vary in type from the heavy "Jack Johnsons" to the hand bomb, and all the wounds caused by these are ragged and attended with loss of tissue with an area round the wound necrotic and devitalized. Fragments of shell are rough and jagged, and carry with them into the wounds highly septic material, along with portions of clothing, mud, etc.

The added difficulty experienced in collecting the wounded, with the result that they have sometimes to lie for long unattended, wet and covered with mud, explains the difficulty in getting rid of much of the wound infection.

These altered conditions in modern warfare have produced changes in the opinions of surgeons as to the treatment of wounds. One change clearly indicated is that the aseptic surgery to which we are accustomed in civil hospitals has not first place in military surgery. In exceptional cases the wound is of such a nature that if not interfered with it heals without suppuration or constitutional disturbance if painted with Tr. iodi. and the first field dressing applied, but this cannot be relied upon. The antiseptic treatment of wounds is up to the present limited in its usefulness—Lister recognized that it was of the greatest prophylactic, but of little curative value. There should, in consequence of his work, be no doubt that in the early stages of wound treatment the antiseptics indicated by him are capable of dealing with sepsis so long as the organisms have not gained an entrance into the deeper tissues. But it is only under these conditions that they are useful. In employing antiseptics sufficiently powerful to destroy organisms implanted in a wound, as he pointed out, these chemical substances also lower or even destroy the vitality of the tissues with which they come in contact, and so may provide a more suitable and extensive field for the further development of the organisms for whose destruction they are employed. The antiseptic chosen in the early stages of treatment is of importance. It has been our practice in recent wounds, both of bone and soft parts, to swab the wound freely with pure carbolic acid, packing it afterwards for
Treatment of Wounds by Magnesium Sulphate

twenty-four hours with gauze steeped in carbolic lotion (one in twenty). This together with free and dependent drainage has been frequently successful in obviating or minimizing sepsis. This is followed at the end of twenty-four hours by the application of the magnesium sulphate treatment to be described later. Recently there has been a tendency to rely on hypochlorous acid, in the form of eusol, or Dakin's solution, as an antiseptic, and it is said that either, while exercising a powerful bactericidal effect when brought in contact with infected tissues, has no injurious effect upon them.

Their usefulness, like that of all antiseptic substances, is probably limited to cases in their early state and, so far as our experience guides us, they are not good throughout the course of treatment.

Attention has been drawn by Sir Almroth Wright and others to the employment of hypertonic solutions, i.e., substances which produce a copious flow of lymph from the tissues with which they come in contact and by causing a vis-a-tergo, wash the discharges and organisms out of the wound, dilute the toxins, and render them comparatively harmless.

It is to our practice for early infected wounds treated as soon as possible in France, and later in septic and suppurating cases in England by magnesium salts in various dilutions, that we seek to draw attention.

From a clinical point of view hypertonic solutions, to produce their ideal results, must have the following properties:

1. They must not be easily absorbed.
2. They must stimulate the growth of granulations in the whole of the wound and these granulations must be firm, compact and vascular.
3. Their applications to wounds must be simple and easy, and the changing of dressing containing them infrequent and painless.

The application of magnesium sulphate fulfils these requirements. It is not absorbed, the granulations formed under it are ideal, the dressings, even in the most septic cases, need only be changed twice a day, and its use is painless. It has the additional advantage of being cheap, readily procured, and easy to handle.

Lieutenant Tulloch has undertaken much experimental work, and his results, recorded later, offer, in addition to points of clinical interest, experimental evidence of the value of magnesium sulphate as a surgical dressing in septic cases.

In no case so treated has there been any symptom of absorption (pain, thirst, diarrhoea, rise in temperature).
Secondary abscesses and lymphatic infections have not occurred. Many patients have expressed their satisfaction as to the painlessness of the dressings. The only instance in which a suspicion of absorption arose was the following case:

Pte. E. B. was admitted into the Northumberland War Hospital on September 14, 1915, suffering from a wound of the left gluteal region, which was supposed to have penetrated the abdomen. Abdominal section was performed on August 26 in France for peritonitis.

On admission: There was a wound the size of a threepenny-piece in the left gluteal region, and a large granulating wound about the size of the palm of a hand in the middle line of the abdomen below the umbilicus. The margins of the abdominal wound had been drawn together with sutures, but had broken down, and in the centre of the wound was a fistula discharging faecal matter in such quantities that the wound had to be dressed five or six times a day. The surrounding skin was raw and ulcerated. The abdomen was flaccid, and the patient did not complain of pain. Magnesium sulphate dressings were applied, and ordered to be changed twice daily. Oleate of zinc ointment was applied to the excoriated skin.

September 20: The wound had cleaned up considerably, the granulations were healthy, and the wound was closing in. October 1: Patient complained of diarrhoea coming on about every two hours. It had no reference to food, and as it was thought it might be due to absorption of magnesium sulphate, the dressings were changed to spirit gauze and wool, but as this produced no cessation of the diarrhoea, he was carefully dieted, and chlorodyne and bismuth given medicinally. This arrested the diarrhoea. The magnesium sulphate dressings were reapplied, and there were no further symptoms.

October 29: Wound quite healed, but there was a space between the recti muscles filled in only by peritoneum and dense scar tissue. January 8, 1916: The scar was excised by an elliptical incision, and, in doing this, the peritoneum was opened at the upper angle of the wound. The anterior rectus sheaths on each side were incised through the whole length of the incision, about ½ inch from the middle line. The opening in the peritoneum was closed with a continuous catgut suture, and the two inner flaps of rectus sheath with figure-of-eight sutures of the same material, so that this portion of the sheath covered the whole of the exposed peritoneum. The rectus muscles, with the outer portions of their sheath, were brought together with quilted sutures of catgut, and a finer continuous suture of catgut approximated the edges. The skin was
380 Treatment of Wounds by Magnesium Sulphate

closed with silkworm gut sutures and horsehair. The wound healed, and except for slight subcutaneous haemorrhage caused no further trouble.

The type of granulation produced by magnesium sulphate is such that very little absorption is possible from it. A sloughing suppurating wound is converted under it in a few days to a bright red flat, compact, granulating surface, which lends itself to the rapid growth of epithelium from its edges. In deeper wounds, and where the bone is injured or laid bare, a similar result may be anticipated. It is the rule that sepsis is held in check, suppuration disappears, healthy granulations soon cover the bare bone and tendons, and the amount of necrosis is diminished or even entirely prevented. The following cases may be offered as ordinary examples:

Gnr. G. W. was admitted into the Northumberland War Hospital on August 17, 1915, suffering from a gunshot wound of the head. The notes supplied accompanying him from France were: “August 7: Shell wound right parieto-frontal region with small gutter fracture of bone. Osseous lesion slight, involving only the outer table. No injury to inner table. Dura intact and brain pulsating well. Had slight weakness of left leg and loss of abdominal reflexes on the left side probably due to concussion.”

On admission: There was a wound, about 1 1/2 inch long, unhealthy, and suppurating profusely over the right fronto-parietal region. Encircling this was a horseshoe-shaped incision with base anterior, the operation wound. The flap was as large as the palm of a hand. The stitches were still in situ, and two drainage tubes passed right under the flap. The stitches and drainage tubes were removed, and the wound was opened up in its entirety. The whole of the exposed bone, about 4 inches by 3 inches, was white and bare. Lint steeped in magnesium sulphate solution was loosely packed under the scalp. The whole wound was covered with lint wet in the solution, with jaconet and absorbent wool superimposed. It was ordered to be dressed twice a day. August 21: The wound was much cleaner, discharge less profuse, and granulations were showing in places on the bare bone. As we were at this time trying magnesium chloride solution of strength 1 to 8 on all septic cases in our wards, this was substituted for the sulphate solution. August 25: Wound much cleaner, but granulations more flabby, and bled more freely. Stronger solution (1 to 4) of magnesium chloride applied. August 27: Patient developed a sharp attack of erysipelas of scalp and face. Dressings changed to magnesium sulphate solution, and lint steeped in it applied to the whole face and
J.S. admitted 12: X:15:

First drawing, Oct. 15th 1915.

Second drawing, Oct. 23rd 1915.

Exposed Tendons
Bone
Slough
Healthy Granulations
Tendons
Bone
Granulations

head. For some days the patient was seriously ill, with high temperature and delirium, but gradually the attack subsided, and on September 30 he was able to be out of bed.

From the date of the reapplication of magnesium sulphate, the wounds rapidly improved, pus disappeared, healthy red firm granulations covered the exposed bone, none of which was lost by necrosis. When the whole bone was thus covered, the scalp flap was replaced, and by October 30 the wound was entirely healed.

The development of erysipelas in this case decided us to give up the magnesium chloride and return to the magnesium sulphate in all cases.

It seemed to us that in the presence of weak, flabby granulations, such as the chloride produces, absorption of fluids is probable, and the passage of organisms becomes easy.

If free and dependent drainage is made, and the wound packed loosely with lint soaked in magnesium sulphate solution, the necessity for drainage tubes no longer exists, for the hypertonic action is such as to wash out discharges from the wound, prevent the formation of pus, and establish a healthy granulating surface.

The growth of epithelium from the edges of the wound is stimulated, the resulting scar is firm and mobile, and very little contraction takes place. (See diagrams.)

Pte. J. S. was admitted into the Northumberland War Hospital on October 12, 1915, suffering from a wound on the left hand caused by the bursting of a bomb.

On admission: There was an extensive lacerated wound on the inner and back part of the left hand. The metacarpal bone of the little finger had been almost entirely blown away, and the extensor tendons were freely exposed. The skin was hanging loose into the sloughing, gaping wound. He could move all the fingers slightly except the little finger, but could not move the wrist joint.

X-ray examination showed the proximal end of the fifth metacarpal bone missing. There was also a fracture of the unciform bone. The wound was dressed with magnesium sulphate dressings, and the drawings show the subsequent progress of the case. Several small sequestra were removed on January 5, 1916, and the wound healed rapidly. The little finger remained frail and useless.

The healthy granulating surface also formed a good, aseptic, vascular base for skin grafting.

Lance-Cpl. A. M. was admitted into the Red Cross Hospital on September 28, 1915, suffering from a shell wound of abdominal wall. On admission there were three wounds, the largest on the right
Treatment of Wounds by Magnesium Sulphate

side of the abdomen below the costal margin, about the size of a cheese plate; a second below this in the right iliac fossa and a third in the right groin. None of them were deep. All were suppurating freely.

 Treatment.—Magnesium sulphate dressings were applied and on October 27, when healthy granulations existed, the wounds were covered with Thiersch skin-grafts taken from the right thigh. A cage of perforated zinc was fastened over the grafts and a sterile towel over the top of this so that no direct dressing was applied to the grafts. On November 5: cage removed, all grafts were holding and a dressing of weak ichthyol ointment was applied. November 25: patient discharged from hospital.

The dressing of septic wounds is not as a rule easy and is accompanied by special discomfort and pain to the patient so that complicated apparatus and frequent changing of dressing, anything that causes more than ordinary inconvenience, is undesirable and may be harmful.

The application of sulphate of magnesium dressing is painless and easily carried out and the dressings, even in the most septic cases, need only to be changed twice a day.

The condition of the wounds when convoys arrive from overseas demands attention. The dressings generally consist of gauze which has been moistened with some solution and covering it a quantity of cotton wool. The wound, soon after the application of such a dressing, becomes dry from evaporation, so that difficulty is experienced and pain caused by removing the dressings which have become adherent to the wound. In the deeper wounds discharges are pent up and the condition of the patient and the wound suffer. The simplicity of application of magnesium sulphate, and the infrequent changes of dressing necessary, allows of several cases being attended to in a short time, and makes it the ideal dressing for wounds where the transport of the patient is necessary, and these deleterious results are likely to happen.

Mode of Preparation.—A saturated solution of the salt has given the best results, both clinically and experimentally—forty ounces of magnesium sulphate (by weight) are dissolved in ten ounces of glycerine and boiling water sufficient to make a Winchester quart (by measure). The glycerine must be added slowly while the solution is hot and stirred gently or the salt precipitates on cooling. The solution is then sterilized in an autoclave and is ready for use.

Application as a Dressing.—In recent injuries the wound is
freely opened up, any foreign body, bullet, portion of shell, clothing, etc., is removed and the whole wounded surface is swabbed over with pure carbolic acid. In the case of fractures, the ends of the bone are treated in the same way, and free fragments of bone are removed. The wound is gently packed for twenty-four hours with gauze wrung out of carbolic lotion (1 in 20) and antiseptic wool applied as an outer dressing. At the end of this time, the wound is dressed, the gauze plug is removed, the wound is syringed out with magnesium sulphate solution of the strength indicated above, no swabbing of the wound is done and the wound is loosely packed with sterile lint taken out of the magnesium sulphate solution in which it is constantly kept. The strips of lint used are narrow (from half inch to one inch wide) so that the solution with which they are saturated comes in contact with all parts of the wound surface. A double layer of lint, wet with the solution, covers the whole of the surface wound. This is covered with a piece of jaconet and then cotton wool, the whole dressing being fixed loosely by a bandage. In the case of wounds of a later date, where sepsis and suppuration are fully established, the treatment by carbolic acid is omitted and magnesium sulphate solution is commenced at once. Dressings even in the worst cases are changed only at twelve hours intervals thus saving a patient much discomfort and trouble. The effect on the wound is very striking. In two or three days pus has almost disappeared, sloughs begin to separate, and the whole surface presents a bright red colour. The granulations never become flabby or oedematous, but instead a firm, vascular, healing wound is seen. Scratching the surface of the wound with a probe hardly disturbs the vascular granulations. The growth of epithelium from the edges of the wound proceeds vigorously and the treatment may be continued with advantage until the entire wound is healed. The resulting scar is firm and elastic and seldom tends to contract or to become painful.

Pte. A. B. was admitted into the Red Cross Hospital on March 22, 1915, suffering from an injury to the left leg. A posterior splint was applied to the leg during transport from France and on removing the dressings, pus poured from a wound in the back of the leg. A drainage tube passed under a bridge of skin and muscles in the middle of the calf, and a large gaping wound was present on the inner side of the calf muscles. He stated that a large piece of shell had passed right through the calf of the leg. No fracture could be found on examination or by X-rays.

_Treatment._—The leg was slung on a cradle, the drainage tube
removed and the wound lightly packed with lint wrung out of magnesium sulphate solution. Progress made was very rapid, the wound soon healed and on April 30 he was discharged to a convalescent home with the wound quite healed and a mobile scar.

In some cases where the dressing has extended over the skin surrounding the wound, pustules appear from some irritating effect of the solution on the skin glands. To prevent this occurring the lint should not much more than cover the wound, or the neighbouring skin may be smeared with oleate of zinc ointment.

We tried in a series of cases diluting the solution a half, a quarter, and an eighth, and also substituting magnesium chloride in half the strength of sulphate (1 in 4); but on every occasion on which this was done pus again appeared in the wounds, granulations became flabby, weak and edematous and bled too freely when touched. On returning to the stronger solution the wound again resumed a healthy appearance. The laboratory experiments by Lieutenant Tulloch largely explain the results of the clinical findings.

Constitutional symptoms seldom occur, probably owing to the fact that owing to the density of the granulations absorption does not take place. There is therefore no general disturbance of health. There is an absence of lymphatic and glandular infection and secondary abscesses have been in my experience unknown.

The effect in the majority of compound fractures is very quickly manifest. Pus rapidly disappears and the amount of necrosis in comminuted cases appears, as would be expected when infection is diminished, to be materially less.

In the wards about a Winchester quart of the solution is used every day in dressing about forty cases, and the cheapness of the lotion, with the infrequent dressings required, means no inconsiderable saving of expense.

Investigation of Magnesium Sulphate Solution with a View to its Employment in the Treatment of Septic Wounds.

(By Lieutenant W. J. Tulloch.)

Solutions of salts are at present so extensively used in the treatment of wounds that a number of problems presented by their employment are worthy of consideration.

So far the salt that has naturally received most attention in this connexion—thanks to the brilliant work of Sir A. E. Wright—has been sodium chloride, presumably because it is the predominant electrolyte of the tissues and its use as an "osmotic cleanser" is therefore regarded as free from danger.
While the value of NaCl as an inducer of "lymph lavage" cannot be gainsaid, it appears questionable if it is the best "osmosing" solution that could be made use of, for, in addition to the power of producing lymph flow by osmosis, certain other properties of the solutions employed have to be considered. Among these may be cited the following:—

1. Its influence on the proteolytic action of pus.
2. The extent to which the salt is absorbed by granulations.
3. The effect of the salt on phagocytosis.
4. The type of granulation produced.
5. The influence of the salt on the bacterial flora of the wound.

Of these, the second, third and fourth are interdependent and their relation to a wound infection is of supreme importance, in that a barrier of compact healthy granulations is the best safeguard that the tissues can have against bacterial invasion, with its sequelae of secondary abscess formation and spreading infection of the wound area.

If the salt used for producing osmosis be absorbed the danger of causing the granulations to become soft and puffy is not negligible.

Among the less readily absorbed salts MgSO₄ is prominent and the following experiments have been undertaken with a view to determining its properties in respect of surgical therapeutics.

**Method Employed for Standardizing the Solutions Used.**

The basis upon which the solutions employed were standardized is as follows:—

The concentration of magnesium sulphate employed by Mr. A. E. Morison in his wards was considered as unity, and a series of dilutions of salts—NaCl, MgCl₂, Na₂SO₄—of equiosmotic value was prepared. The equiosmotic power in each case was arrived at by the method of Hamburger [1]. It was found that a solution of approximately twelve per cent NaCl had to be diluted with the same bulk of water as had the solution of MgSO₄ employed to render both isotonic with human blood corpuscles.

The solutions of the salts were made in series, halving the concentration in each successive tube so that in a series of six tubes—"a" to "f"—of the MgSO₄ solution, we had "a" equal to 1, "b" = 1/2, "c" = 1/4, "d" = 1/8, "e" = 1/16 and "f" = 1/32 of the strength of solution which had been employed in wound treatment, while in the NaCl series "a" was equal to 4, "b" to 2, "c" to 1, "d" to 1/2, "e" to 1/4, and "f" to 1/8 of the strength of Wright's
hypertonic saline, assuming this to be a three per cent solution of salt.

In each experiment, corresponding series of Na$_2$SO$_4$ and MgCl$_2$ were also examined, the object being to determine if possible the action of the ions Mg, Cl, Na, and SO$_4$ as distinct from the molecules of MgSO$_4$ and NaCl.

(1) Experiments relating to the Influence of Salts on the Proteolytic Action of Pus.

It is known that pus has proteolytic properties, and if left in contact with a wound interferes to some extent with the growth of new tissue. This interference however, is of but little import where highly vascular tissue is concerned for such tissue contains sufficient serum to inhibit this proteolytic activity, and largely to negative its ill effect. Ordinarily proteolysis is of importance because it interferes with epithelialization, when the avascular and therefore not antiproteolytic epithelium experiences difficulty in growing in presence of pus.

If then the magnesium sulphate dressing is to be used as a fomentation, and unless it can be so used it has little advantage over salt, it must interfere with this proteolytic activity of the wound exudate.

The first series of tests was carried out with a view to investigation of this point.

**Series No. 1.**

**Experiment No. 1. Influence of the Salts on Tryptic Digestion.**—Before carrying out the experiment the dose of trypsin necessary for complete digestion—in one hour at 50°C.—of that quantity of protein suspension employed in the tests was determined, the reactions being carried out in 0.9 per cent NaCl plus 0.5 per cent Na$_2$CO$_3$.

Using twice the dose of trypsin as ascertained by the above procedure, and working under the same conditions in the presence of varying dilutions of the salts, the following result was obtained:

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<td>MgSO$_4$ (as used in the wards)</td>
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<td>NaCl (equiosmotic with MgSO$_4$)</td>
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<td>MgCl$_2$ (equiosmotic with MgSO$_4$)</td>
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<tr>
<td>Na$_2$SO$_4$ (equiosmotic with MgSO$_4$)</td>
<td>p</td>
<td>x</td>
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x = complete digestion of the protein.
= no digestion.
p = partial digestion.
These results proved that the Mg salts markedly interfere with the action of trypsin. This seems to depend on the Mg ion, and it is not improbable that other divalent cations would have a similar effect. This point, however, has not been investigated.

The experiment is suggestive, but is open to the obvious criticism that trypsin is not pus and the mechanism of proteolysis by pus may well be different from that of trypsin proteolysis, just as the mechanism of peptic digestion differs from that of trypsic digestion.

Series No. 2.

Effect of the Salts on Leucocyte Ferments.—In view of the above criticism other methods were devised to show the influence of the salts on the ferment activity of leucocytes.

A few preliminary tests were made employing a technique similar to that of the Abderhalden test, but owing to the supply of ninhydrin running short sufficient observations could not be made to permit of any conclusions being drawn from the work done.

It was then decided to make use of the method described by Wright for investigating the “antitryptic” action of serum in further examination of the problem.

A thirty per cent peptone gelatine standardized to plus 20 of Eyre’s scale was used as the material to be digested. This concentration of gelatine was chosen so that with the addition of an equal volume of electrolyte to be examined the strength of the gelatine equalled fifteen per cent (plus ten of Eyre’s scale).

The obtaining of sufficient leucocytes free from serum was a problem that presented some difficulty, and after a few preliminary examinations it was decided to employ washed clot as the source of the leucocyte ferments.

Blood, obtained with care to prevent gross contamination was set to coagulate overnight, the clot was then washed in sterile water, forced through a fine sieve into a large volume of sterile water—temperature about 40° C.—contained in wash-bottle flask. Before proceeding to wash the clot the total weight of blood was determined and a known fraction of this was treated in the same way, its residue after washing being weighed in order to estimate the weight of washed clot obtained from the blood.

The fluid in the flask was renewed several times and the flask was shaken until the clot became almost colourless. The water was then run off and the deposit of washed clot was smeared over the interior of the flask by means of a sterile glass spatula; the flask was then inverted and the excess of water allowed to drain off.
For each 0.5 grammes of washed and drained clot in the flask one cubic centimetre of thirty per cent gelatine was added and the whole well mixed. This constituted a "clot-gelatine mixture" which could be used in this series of experiments, and of this mixture 1.5 cubic centimetres were added by means of a wide-mouthed pipette to an equal volume of the solutions of salts to be investigated.

Experiment A.—In this experiment human clot was used, the above quantities of the reagents being employed. The clot was obtained from the pooled blood of cases examined by the Wassermann test, all the blood samples employed having given negative reactions.

After mixing the reagents the tubes were incubated at 50ºC. for twenty-four hours, removed from the incubator, and then placed in water at 7ºC. for two hours to harden the gelatine before readings of the experiment were taken.

The following result was obtained:

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<th>MgSO₄</th>
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At forty-eight hours:

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<th>Na₂SO₄</th>
<th>MgCl₂</th>
<th>NaCl</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

x = gelatine on cooling still sets.
- = gelatine liquefied.
* = result not satisfactory, or no definite result.

The above results suggest that of the salts examined, MgSO₄ only has an inhibitory influence in the conditions under which the experiment was performed on the liquefaction of gelatine by leuco-
cyte ferments, but the evidence, while suggestive, is not conclusive, for it may be that the result depends largely upon the influence of the electrolytes themselves upon the gelatine. The fact that liquefaction has occurred only in the presence of the higher concentrations of the salts points to this, although controlled experiments (vide Experiment B) suggest that some factor other than the electrolytes must be considered as taking a part in the liquefaction.

That salts alone have a marked effect on gelatine is well known. "Saline digestion of gelatine" is a phenomenon long recognized, and it would appear from the experiment under consideration that the converse may occur, both Na₂SO₄ and MgSO₄ tending to harden gelatine. This hardening effect masks the digestion in presence of Na₂SO₄ until incubation has been in progress for three to four days.

It will be noted that in the above experiment the highest concentration of the salts are equal to six per cent NaCl, not twelve per cent as in the experiments of the other series, and in the trypsin experiment first described. The concentrations were reduced so that the effect of the salts alone upon the gelatine would vitiate the results to a less extent than would have been the case were the highest concentrations used. Strong solutions of NaCl markedly interfere with the setting of gelatine, liquefying it in neutral solution, and precipitating it in presence of acid.

It is interesting to note in this connexion that Rubinstein [2], investigating the "antipeptic" influence of blood salts, found that Na₂SO₄ and NaCl had no "antipeptic" properties, while the phosphates of magnesium and calcium were very active, the former being five times as active in inhibiting peptic digestion as the latter. It is only fair to relate in this connexion that the findings of Grutzner and Pfleiderer do not agree with those of Rubinstein in respect of the influence of Na₂SO₄ on peptic digestion.

Experiment B.—As the results of Experiment A of this series were open to criticism on the ground that the test was performed at 50°C., another series was set up using the same technique, but substituting washed sheep clot for washed human clot and incubating at 37°C.

Here greater difficulty was experienced in obtaining clot free from gross contamination than was the case when human clot was employed, and the technique had to be so modified that growth of contaminating organisms could be inhibited at 37°C. This was done by incubating the tubes in a metal box, the floor of which was covered with cotton wool on which was sprinkled ten cubic
390 Treatment of Wounds by Magnesium Sulphate

centimetres of chloroform, after which the lid was sealed down with plasticine. Tubes of broth sown with Bacillus coli, B. subtilis, and Staphylococcus aureus were incubated along with the gelatine tubes to ensure that the chloroform vapour employed sufficed to prevent the growth of these organisms.

Employing this method the following results were obtained, the experiments with the clot present being controlled by a similar series of tubes containing no clot.

After twenty-four hours' incubation at 37° C.:

<table>
<thead>
<tr>
<th></th>
<th>Without clot</th>
<th>With clot</th>
</tr>
</thead>
<tbody>
<tr>
<td>MgSO₄</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>Na₂SO₄</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>NaCl</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>MgCl₂</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
</tbody>
</table>

After forty-eight hours' incubation:

<table>
<thead>
<tr>
<th></th>
<th>Without clot</th>
<th>With clot</th>
</tr>
</thead>
<tbody>
<tr>
<td>MgSO₄</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>Na₂SO₄</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>NaCl</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>MgCl₂</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
</tbody>
</table>

After seventy-two hours' incubation:

<table>
<thead>
<tr>
<th></th>
<th>Without clot</th>
<th>With clot</th>
</tr>
</thead>
<tbody>
<tr>
<td>MgSO₄</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>Na₂SO₄</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>NaCl</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>MgCl₂</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
</tbody>
</table>

After ninety-six hours' incubation:

<table>
<thead>
<tr>
<th></th>
<th>Without clot</th>
<th>With clot</th>
</tr>
</thead>
<tbody>
<tr>
<td>MgSO₄</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>Na₂SO₄</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>NaCl</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>MgCl₂</td>
<td>x x x x x x x</td>
<td>x x x x x x x</td>
</tr>
</tbody>
</table>

x = gelatine solidified.
— = gelatine not solidified.
p = gelatine fluid, but markedly viscous.

The observations in this experiment were made under the same conditions as in the previous test and the above result (after four
days' incubation) was verified by allowing the tubes to set overnight. The result was the same as that noted, but in the Na₂SO₄ series "with clot," the liquefied gelatine was more viscous than in the case of the chlorides.

This experiment was repeated several times, both at 37° C. and 50° C., and the results, while not absolutely constant, all showed the following points in common:

(a) The controls did not show liquefaction.
(b) In presence of the higher concentrations of the chlorides the gelatine was liquefied if clot was present.
(c) The Na₂SO₄ series was always difficult of interpretation, there being no liquefaction till the third day.
(d) Liquefaction, unless exceptionally, did not occur in presence of MgSO₄ and then only in presence of the lowest concentration examined.

These results suggest that MgSO₄ has an inhibitory influence upon the digestion of gelatine by blood clot—a property not shared by the other salts examined—but the conditions of the reagents in the tubes in these experiments are so complex that a slight alteration in the conditions of the test might lead to very different results.

I therefore hesitate to draw any definite conclusions from these experiments even though, as indicated above, the findings are fairly constant, and I believe that a more satisfactory indication of the antiproteolytic properties of MgSO₄ is to be found by observation of the comparative rates of epithelialization of wounds treated by MgSO₄ and hypertonic salt.

(2) Note Concerning Absorption of MgSO₄.

Although we cannot offer definite evidence to the effect that MgSO₄ is not absorbed by granulation tissue we have good grounds for believing that absorption of this salt, if it occurs at all, is so slight as to be almost negligible.

Physical chemistry suggests this. Hober [3] showed that Mg ion was the slowest in passing through animal membranes—such as intestine—of all the cations he examined. Na ion passed through much more rapidly.

He also found that of the anions Cl was the most, and SO₄ the least absorbable of the ions investigated.

Pharmacology, too, indicates that the action of MgSO₄ in the intestine at least, is mainly osmotic, the salt not being absorbed.

As definite experimental evidence on the point under considera-
Treatment of Wounds by Magnesium Sulphate

...tion is lacking, I shall not further elaborate this section of the work, but desire to call attention to the following points.

The granulations in wounds treated with MgSO₄ do not tend to become flabby and there is little pain associated with the treatment. Both these facts suggest that absorption does not take place.

The employment of NaCl in comparison causes considerable pain, and of a number of cases thus treated the granulations tended to become redundant.

As illustration of this point I may cite the experience of Major D'Oyly Grange, Surgical Registrar, Northumberland War Hospital, who finds that not infrequently treatment by continuous irrigation with three to five per cent NaCl results in the granulation tissue becoming oedematous. The oedema may be transient and is soon reduced when the three per cent NaCl solution is replaced by 0.75 per cent.

This oedema probably arises thus: Salt is absorbed by the superficial granulations which then become "hypertonic" to the underlying tissues; should the fluid from the deeper tissues pass at a greater rate to these granulations than the fluid is withdrawn from them to the solution bathing the wound surface, a condition of water stasis will ensue. Though clinical evidence indicates that in most cases the stasis is but temporary and an equilibrium is soon established, nevertheless NaCl is being absorbed all the time that NaCl dressings or irrigation fluids are in contact with wounds. I think that this is a point of great importance, for largely upon it depends our thesis that MgSO₄ presents advantages over NaCl as an "osmotic cleanser" of wounds. Not being absorbed it in no way interferes with the vital activities of the cells of granulation tissue.

We have used MgCl₂ in a few cases but this salt was found to answer less satisfactorily than MgSO₄. I believe that it is less satisfactory because it is more readily absorbed than MgSO₄.

(3) Influence of Salts on Phagocytosis.

It is my belief that MgSO₄ has a distinct advantage over NaCl, as, by virtue of its not being absorbed, it will not interfere with the phagocytic activity of living leucocytes.

It is well known that phagocytosis is not so active in presence of hypertonic solutions of NaCl as it is in isotonic saline, and in employing NaCl, which is readily absorbed, there is a risk of interfering with the phagocytic power of the leucocytes in the granulations.

Our aim should be to obtain a dressing which would not interfere with the digestive and phagocytic activities of the white cells so...
Albert E. Morison and William J. Tulloch

long as these are constituents of living tissue, but one which will inhibit their proteolytic power when the leucocytes escape and become part of the purulent discharge.

The following opsonic estimations show the effect of the salts under consideration on the power of phagocytosis.

Opsonic tests were set up as follows:

(1) Tube "a"—Equal volumes of *Staphylococcus aureus* emulsion, washed leucocyte suspension, serum, and twelve per cent salt were mixed and incubated at 37° C. for fifteen minutes, a slide was then prepared in the usual way and a count of organisms in 100 leucocytes was made. The staphylococcus and leucocyte emulsions were both prepared in 0:85 per cent NaCl. In this tube then the NaCl = 3:65 per cent.

(2) Tube "b"—Prepared in the same way but the twelve per cent NaCl was replaced by six per cent. The NaCl concentration = 2:06 per cent.

(3) Tube "c"—As before, but three per cent NaCl used in place of twelve per cent NaCl concentration = 1:31 per cent.

(4) Tube "d"—As before, but 1:5 per cent NaCl used = NaCl concentration = 0:93 per cent.

(5) Tube "e"—Used 0:75 per cent—Concentration of NaCl = 0:75 per cent.

(6) Tube "f"—Used 0:375 NaCl—Concentration of NaCl = 0:63 per cent.

A similar series of tubes each containing MgSO₄ in place of the NaCl—12 per cent, 6 per cent, 3 per cent, 1:5 per cent, 0:75 per cent, 0:375 per cent—was set up and dealt with in exactly the same way as were the NaCl series, for comparison with these.

Employing this technique the following results were obtained, the numbers indicating the cocci phagocytosed per leucocyte in the count of 100 cells:

<table>
<thead>
<tr>
<th>NaCl Per cent</th>
<th>MgSO₄ Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;a,&quot; 3:65, ingested organisms = 0:04</td>
<td>&quot;a,&quot; equiosmotic with 3:65 NaCl, ingested organisms = 0:00</td>
</tr>
<tr>
<td>&quot;b,&quot; 2:06, &quot; &quot; = 0:26</td>
<td>&quot;b,&quot; 2:06 &quot; &quot; = 0:18</td>
</tr>
<tr>
<td>&quot;c,&quot; 1:31, &quot; &quot; = 1:2</td>
<td>&quot;c,&quot; 1:31 &quot; &quot; = 0:7</td>
</tr>
<tr>
<td>&quot;d,&quot; 0:93, &quot; &quot; = 5:7</td>
<td>&quot;d,&quot; 0:93 &quot; &quot; = 5:1</td>
</tr>
<tr>
<td>&quot;e,&quot; 0:75, &quot; &quot; = 9:36</td>
<td>&quot;e,&quot; 0:75 &quot; &quot; = 8:5</td>
</tr>
<tr>
<td>&quot;f,&quot; 0:63, &quot; &quot; = 13:3</td>
<td>&quot;f,&quot; 0:63 &quot; &quot; = 14:1</td>
</tr>
</tbody>
</table>

These results are interesting because they show that even a moderate increase in the tonicity of the fluids causes some inhibition of phagocytosis.

I was surprised however, that MgSO₄ did not cause more marked
inhibition than was the case, for it appeared not improbable that
the Mg ion would exert a toxic influence, apart from the influence
of increased tonicity, in respect of the phagocytic process.

The point is only of minor import however, as the non-absorption
of MgSO₄ would rule out any deleterious effect caused through this
mechanism.

(4) Type of Granulation Produced.

The granulations resulting after the MgSO₄ treatment are flat,
compact, and vascular, making a formidable defence against
organismal invasion of the surrounding tissues. These character­
istics must be associated with the absence of absorption of the
salt for reasons indicated in the preceding section.

It is also important to remember that, being compact throughout
the course of treatment almost from its inception, the granulations
form a good scar, which is remarkably mobile, and does not tend to
contract so much as an ordinary scar of a similar size would
certainly do.

(5) The Effect of MgSO₄ and Solutions of other Salts (Equiosmotic)
with MgSO₄ Solutions on the Growth of Organisms Infecting
Wounds.

A final series of experiments was carried out to determine the
influence of NaCl, MgSO₄, Na₂SO₄, and MgCl₂, upon growth of
the organisms commonly found infecting wounds.

Broth containing 2 per cent peptone was used to dilute the
solutions which were made equimolecular with 12 per cent, 6 per
cent, 3 per cent, 1·5 per cent, 0·75 per cent, and 0·375 per cent
NaCl in each series. To each of the tubes containing these con­
centrations of electrolytes there was added one cubic centimetre
(equal volume) of broth heavily inoculated with the organism to be.
examined. The tubes were then incubated for twenty-four hours
at 37° C., and examined both macroscopically and by film
preparations.

Experiment A.—Examining in this way a streptococcus of the
"pyogenes" type, isolated recently from a wound, the results shown
in the table were obtained.

These results show that both MgCl₂ and MgSO₄ exert a
restraining influence on the growth of streptococcus greater than
do NaCl and Na₂SO₄. This effect appears to depend on the
Mg ion, for experiments in which the gradation of concentrations
was less abrupt showed that MgCl₂ was more active than MgSO₄—
a result that one would expect in view of the more marked dissociation of the chloride.

<table>
<thead>
<tr>
<th>NaCl concentration</th>
<th>NaCl</th>
<th>MgSO₄</th>
<th>Na₂SO₄</th>
<th>MgCl₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 per cent</td>
<td>No growth; good growth; normal appearance</td>
<td>No growth; normal</td>
<td>No growth; good growth; normal appearance</td>
<td>No growth.</td>
</tr>
<tr>
<td>3 &quot; &quot;</td>
<td>Good growth; normal</td>
<td>&quot; &quot;</td>
<td>&quot; &quot;</td>
<td></td>
</tr>
<tr>
<td>1-5 &quot; &quot;</td>
<td>Good growth; normal</td>
<td>Fair growth; great variety in shape and staining properties</td>
<td>Good growth; normal</td>
<td>Slight growth; great variety in shape and staining properties.</td>
</tr>
<tr>
<td>0-75 &quot; &quot;</td>
<td>Good growth; normal</td>
<td>Good growth; normal</td>
<td>Good growth; normal</td>
<td>Good growth; normal.</td>
</tr>
<tr>
<td>0-375 &quot; &quot;</td>
<td>Good growth; normal</td>
<td>Good growth; normal</td>
<td>Good growth; normal</td>
<td>Good growth; normal.</td>
</tr>
</tbody>
</table>

In the above experiment, and in those which follow, the highest concentration of the salts is equal to six per cent, the reduction in concentration being due to the addition of the inoculated broth to the dilutions of the salt.

Experiment B.—A similar experiment was carried out with staphylococci, and here none of the salts could be shown to interfere with growth of the organisms.

Experiment C.—In this experiment the organism investigated was B. coli, and the results were peculiar in that very marked involution of the organism occurred in presence of the Mg salts, while, with the higher concentrations of all the salts, the organism developed as a streptobacillus. The involuted forms in the tubes containing the higher concentrations of the Mg salts were very bizarre in appearance, being as much as 30 μ in length and shaped like Higginson enema syringes.

The table, on next page shows the results of the examination of B. coli.

Here, again, is evidence of the inhibitory power of the Mg ion, as shown by the marked inhibition of the growth of B. coli in presence of Mg salts, and notably in presence of the easily dissociated chloride.

Experiment D.—B. pyocyaneus was examined also, but growth took place in the presence of these concentrations of the salts that were tested in this series. The highest concentration of MgCl₂ and MgSO₄ caused some involution of the bacilli. This
slight inhibitory action of Mg, in respect of B. pyocyaneus, could be clearly demonstrated with solutions of double strength of those employed in the experiments of this series.

<table>
<thead>
<tr>
<th>NaCl concentration</th>
<th>NaCl</th>
<th>MgSO$_4$</th>
<th>Na$_2$SO$_4$</th>
<th>MgCl$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 per cent</td>
<td>Poor growth; the bacilli are very large and are arranged in chain formation</td>
<td>Slight growth; organisms are extremely large; are all spindle-shaped, and show great irregularity of staining</td>
<td>Good growth; large in size; show marked chain formation</td>
<td>No growth.</td>
</tr>
<tr>
<td>3  &quot;</td>
<td>Organisms large; arranged in short chains</td>
<td>Fair growth; chain formation; spindle forms in large numbers; stain irregular</td>
<td>Good growth; organisms are larger than normal, but show no chain formation</td>
<td>Very slight growth; all the bacilli are spindle-shaped, and very large.</td>
</tr>
<tr>
<td>1-5  &quot;</td>
<td>Normal ..</td>
<td>Organisms are large, and show marked chain formation</td>
<td>Normal ..</td>
<td>Chain formation; irregular staining; some spindle forms.</td>
</tr>
<tr>
<td>0-75  &quot;</td>
<td>&quot; ..</td>
<td>Normal ..</td>
<td>&quot; ..</td>
<td>Bacilli are large, and show chain formation.</td>
</tr>
<tr>
<td>0-375 &quot;</td>
<td>&quot; ..</td>
<td>&quot; ..</td>
<td>&quot; ..</td>
<td>Normal.</td>
</tr>
</tbody>
</table>

Experiments E. and F.—Two saccharose fermenting diphtheroids obtained from wounds were investigated in the same way, but no inhibitory action was observable.

Experiment G.—I was so struck with the examination of streptococcus (Experiment A of this series) that I decided to inoculate a series of tubes of the four salts with a mixed culture of streptococcus and B. pyocyaneus.

A tube containing twenty cubic centimetres of nutrient broth was heavily inoculated with streptococci (one cubic centimetre of a twenty-four hour broth culture), and lightly with B. pyocyaneus (a very small loopful of a twenty-four hours' broth culture). The broth sown thus with the two organisms was distributed into the series of dilutions of the four salts, and the tubes examined after twenty-four hours, and again after forty-eight hours' incubation at 37° C.

In the MgSO$_4$ and MgCl$_2$ series only pyocyaneus grew in the two highest concentrations and streptococci were very few in number in the tube containing the third highest concentration of these salts, while in the corresponding series of sodium salts the
streptococci were numerous in the second higher concentration and a few could be demonstrated even in the highest concentration.

This aspect of the work was of so much interest that it was decided to make some direct examinations of wound exudates by means of Wright's lymph leeches. Two of these examinations—which were repeated to exclude technical error—are so striking that I feel they are worthy of special note.

(1) Two Wright lymph leeches were applied to a granulating surface known to contain streptococci, and before application each was half filled with sterile solution—one with MgSO₄ as used by Mr. Morison, the other with twelve per cent NaCl. Both leeches were left under the dressing for a period of four hours. On removing the dressings the leeches were transferred to sterile test tubes and incubated from 6 p.m. to 9 a.m. The fluid from each was pipetted into broth which was then incubated at 37° C. for twenty-four hours. The broth inoculated with the contents of the "salt leech" gave a copious growth of streptococci, that inoculated with the contents of the "MgSO₄ leech" gave no growth.

(2) Similar experiments carried out on wounds with mixed infection with streptococci and pyocyaneus gave corresponding results. Both streptococcus and pyocyaneus appeared in cultures from the "salt leeches," pyocyaneus alone in cultures from the "MgSO₄ leeches."

**CONCLUSIONS.**

(1) From the first series of experiments it appears that MgSO₄ exhibits to a greater degree than do the other salts investigated the desirable property of interfering with the digestive activity of pus.

This statement is made with reservation as the experimental methods that one is forced to employ are open to certain criticisms, and I suggest that the rate of epithelialization of the wounds treated would give a truer index of the property than experimental investigation does.

(2) MgSO₄ has not so markedly inhibitory an action on phagocytosis as one would expect and, therefore, even if it be absorbed to a slight extent, it would not have a deleterious influence on the process, while salt, being more readily absorbed, might well interfere with this function of the leucocytes.

(3) Experimental work in physical chemistry and pharmacology points to MgSO₄ as the least absorbable of the readily soluble salts,
Treatment of Wounds by Magnesium Sulphate

while clinical evidence—absence of pain, etc.—points in the same direction.

(4) By virtue of the non-absorption of MgSO₄, the granulations produced are more compact than when a more readily absorbable salt is employed.

(5) The Mg ion has a markedly inhibitory action on the growth of streptococci and B. coli, and a slightly inhibitory effect on the growth of pyocyanus. It has, however, no easily demonstrable influence in the concentrations examined, on the growth of staphylococci, or on the diphtheroids investigated.

Incorporating these conclusions in a final note one may say that it appears from the above findings that MgSO₄ would be the most satisfactory salt to employ for the production of "lymph lavage" and its properties indicate that it might be used satisfactorily and safely in the form of a fomentation.

I lay stress on this last point, for if the fomentations only require renewal twice daily the dangers of manipulation are much reduced and the work of the wards is lightened.

We wish to point out that we do not suggest that MgSO₄ solutions ought to be employed for a first dressing for fresh wounds. These dressings we think should be strongly antiseptic in character, their function being prophylactic rather than curative. It is as a curative dressing in the succeeding phase that we suggest MgSO₄ might be made use of with great advantage.

For permission to publish this paper we are indebted to Colonel G. G. Adams, A.M.S., Commandant of the Northumberland War Hospital.

REFERENCES.