a drowsiness in the patients, and later in some cases there resulted confusion, disorientation, and hallucinations. These psychotic disturbances were, however, temporary, and may be due to anoxia.

In conclusion, then, one may say that the full control of the side-actions of morphine requires the use of three different drugs. N-allylnormorphine (nalorphine) for the control of respiratory depression, although this can be achieved only with the loss of analgesia. Amiphenazole combats central depression and its use is essential for the long-term treatment of intractable pain with large doses of morphine. Experience has shown that very often these large doses of morphine of the order of 600 mg. a day are required to keep the patient completely free of pain. Such treatment has been shown to be absolutely without danger in a series of over 400 cases. Larger doses of amiphenazole (40–100 mg., q.d.s.) than hitherto are now employed. Our wide experience places this drug as one of the safest in medicine. Cyclizine is the drug of choice for the control of vomiting or nausea. This drug is also completely harmless and there is no reason why a patient who experiences even the slightest degree of nausea from morphine (or pethidine) should not be spared the discomfort by a simple and safe treatment, oral medication usually sufficing, although occasionally the intramuscular or intravenous route must be employed.

Summary

Doses of morphine of up to 30 mg. have been given to volunteers and the effects noted. The most frequent side-effect is not respiratory depression but nausea and vomiting, the incidence of which may be as high as 30%. The onset of emesis may be delayed for seven hours. Other side-effects are described.

The nausea and vomiting may be completely controlled by the use of cyclizine chloride.

The central nervous system depression (narcosis) may be controlled with amiphenazole.

Provided the sensitivity of the patient to small doses is first ascertained morphine is not a dangerous drug. All the side-actions can now be controlled.

Large doses of morphine (up to 200 mg., q.d.s.) may be required to control chronic pain. The patient should not be denied the benefit of complete analgesia on the score of side-actions or addiction. The results of over 400 cases show such fears to be groundless when the appropriate antagonist is employed to control the particular side-action experienced by the patient.

We thank the Minister for the Army (Mr. J. O. Cramer) for permission to carry out investigations on Army volunteers and the Australian Army for its whole-hearted co-operation in the investigations. We thank the medical superintendent (Dr. Moon) of the Austin Hospital, for his enthusiasm and untiring attention to our needs, also the sisters and nursing staff for their co-operation. We are grateful to Dr. Kaye Scott for permission to publish the histories of the special cases given in this paper. We would like to acknowledge the assistance given to us by Dr. Noel Cass with respect to the cases in the Second Series. The financial aspect of this work was assisted by a grant from the National Health and Medical Research Council of Australia. We thank Nicholas Pty. Ltd., and Burroughs Wellcome (Australia) Ltd., for generous gifts of daptazole and marzine respectively.

REFERENCES

Ballantine, I. D. (1957). *Lancet*, **1**, 251.
Dundee, J. W. (1957). Ibid., **1**, 376.
Gershon, S., and Shaw, F. H. (1958). *J. Pharm. (Lond.)*, **10**, 22.
Holmes, J. M. (1956). *Lancet*, **2**, 765.
Hügin, W. (1956). *Schweiz. med. Wschr.*, **86**, 1100.
McKeogh, J., and Shaw, F. H. (1956). *Brit. med. J.*, **1**, 142.
Overton, F. C. (1957). *Nursing Mirror*, **104**, March 29, p. XIII.
Robson, J. M., and Keele, C. A. (1956). *Recent Advances in Pharmacology*, 2nd ed., p. 103 Churchill. London.
Shaw, F. H., and Alexander, I. S. In preparation.
Trautner, E. M., Trethewie, E. R., and Gershon, S. (1953). *Med. J. Aust.*, **2**, 848.
Unna, K. (1943). *J. Pharmacol. exp. Ther.*, **79**, 27.
Wechsler, D. (1945). *J. Psychol.*, **19**, 87.
Yates, F. (1936). *J. agric. Sci.*, **26**, 301.

INFLUENCE OF INITIAL VACUUM ON STEAM STERILIZATION OF DRESSINGS*

BY

R. KNOX, M.D., F.R.C.P.
Professor of Bacteriology

AND

E. J. K. PENIKETT, M.B., B.S.
Lecturer in Bacteriology
Department of Bacteriology, Guy's Hospital Medical School, London

It is generally accepted that, in the sterilization of surgical dressings by steam under pressure, air must be efficiently removed from the sterilizer and its contents before steam is admitted. But opinions are divided over the best method of removing air. Most hospital sterilizers are fitted with steam ejectors which draw a preliminary vacuum of 10 in. (25 cm.) Hg or rarely up to 20 in. (50 cm.) Hg but do not reach anything like a vacuum of 29.92 in. (75.97 cm.) Hg which is required for complete removal of air. Perkins (1956) points out the dangers of relying on partial removal of air. He recommends that, instead of drawing a preliminary vacuum, air should be continuously removed by downward displacement through the use of thermostatic valves, ensuring the automatic control of air and condensate discharge. Recently it has been claimed that the most reliable method is to use a pump capable of rapidly producing a vacuum of at least 27–28 in. (68.5–71 cm.) Hg as in some modern German sterilizers (see Bowie, 1957).

Alder and Gillespie (1957) have pointed out that there is remarkably little precise evidence to support the statements that have been made about the merits of different ways of removing air. They measured residual air trapped inside dressings and found that *double* evacuation by means of a steam ejector up to about 20 in. (50 cm.) Hg gave rather more efficient removal of air than downward displacement, but neither of the methods they used could be relied upon to remove air completely, especially when drums were incorrectly loaded.

All those who have studied this problem, whichever method of air removal they recommend, agree that the effect of residual air is to delay the penetration of steam into dressings and so render the attainment of sterilizing temperatures slow and unreliable (Savage, 1937). The time taken to reach an arbitrary sterilizing temperature inside a standard surgical pack can therefore be used as an indicator of the efficiency with which air has been removed before the admission of steam. We have therefore investigated the influence of different levels of preliminary vacuum on the time taken to reach an arbitrary sterilizing temperature in surgical packs deliberately overloaded and badly sited in the sterilizer.

Materials and Methods

A horizontal jacketed autoclave of approximately 11 cu. ft. (0.31 cubic metre) capacity was used (Fig. 1). The steam was supplied at 46 lb./sq. in. (3.23 kg./sq. cm.) after having passed two separators. It was fed to the chamber and jacket independently after passing valves to reduce pressure to

*Report to the Medical Research Council Working Party of Steam-Pressure Sterilization.

20 lb./sq. in. (1.4 kg./sq. cm.). Twenty-seven measurements by calorimetry of the dryness fraction of the steam had a mean value of 0.92 (standard deviation 0.04). This indicated that the steam supply was satisfactory and not far from the ideal condition of dry saturated steam which would have a dryness fraction of 1.00. There was no evidence at any time of superheating within the chamber. In the discharge line a balanced pressure thermostatic type steam trap was fitted. The air was removed with an oil-sealed rotary type piston vacuum pump protected by a water-cooled condenser. Temperature was measured inside the centre of the standard drum described below, by a recording mercury-in-steel thermometer.

Another recording mercury-in-steel thermometer was fitted in the discharge line. Vacuum gauges were of two kinds—one combined with the steam-pressure gauge and reading in inches of mercury, the other a more sensitive instrument reading in millimetres of mercury (absolute pressure). The former was used for moderate vacua and the latter for higher degrees of vacuum. Jacket and chamber pressures were indicated in pounds per square inch by dial gauges as well as recording instruments. All instruments were calibrated at intervals. Preliminary experiments were made to find the position at which the temperature took the longest time to reach 115° C. after steam pressure had reached 20 lb./sq. in. (1.4 kg./sq. cm.). This position was at the bottom in the front of the sterilizer. 115° C. was chosen as the safe minimum temperature for killing *Bacillus stearothermophilus* spores. At 115° C. the spores are killed in 20 to 25 min., but at a lower temperature their killing is much prolonged.

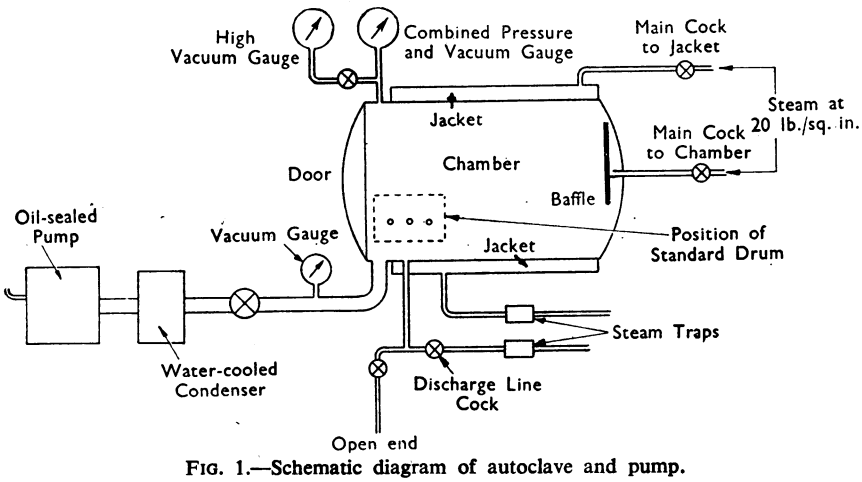

FIG. 1.—Schematic diagram of autoclave and pump.

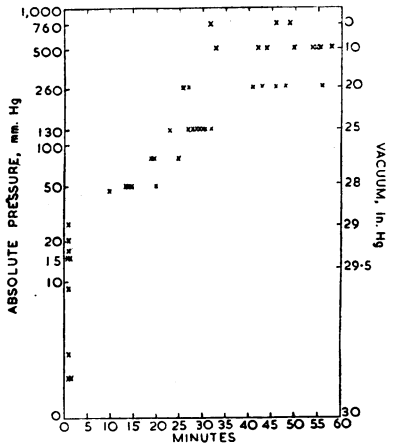

FIG. 2.—Time to reach 115° C. plotted against the initial vacuum. Each × represents a separate experiment.

A drum, 11½ in. (29 cm.) in diameter and 8½ in. (21.6 cm.) high with eight ½-in. (1.3 cm.) diameter ports, was placed on its base in the lower front position. The drum was deliberately placed incorrectly in this way so as to impose a severe test of the efficiency of evacuation. It was lined with two huckaback roller towels and packed with eight 20 by 30 in. (50 by 75 cm.) huckaback hand-towels, each folded to give twelve thicknesses. This was the standard drum. The bulb of a recording mercury-in-steel thermometer was placed in its centre and the capillary packed around tightly to ensure that steam reached the bulb through the load and did not pass along a channel created by the capillary.

The required vacuum was drawn, steam admitted, and the time measured from the moment when the chamber pressure reached 20 lb./sq. in. (1.4 kg./sq. cm.) until the temperature inside the standard drum reached 115° C. In some experiments the time was also recorded for the temperature to rise to the theoretical maximum of 126° C. corresponding to 20 lb./sq. in. (1.4 kg./sq. cm.) of dry saturated steam.

In further experiments the sterilizer was packed to overflowing with towels, bowls, cotton-wool, and loaded drums. A dozen envelopes containing *B. stearothermophilus* and Browne's colour tubes were scattered about the load (Howie and Timbury, 1956). Pressure was reduced to 15 mm. Hg (absolute) and the load exposed to steam at 20 lb./sq. in. (1.4 kg./sq. cm.) for 10 min.

Results

The times taken for the temperature inside the standard drum to reach 115° C. after the chamber pressure reached 20 lb./sq. in. (1.4 kg./sq. cm.) have been plotted against the initial vacuum and are shown in Fig. 2. In all, 43 experiments are recorded. It will be noted that at high initial pressures—that is, low degrees of vacuum—the points were scattered, but with a high initial vacuum—at pressures below 20 mm. Hg (absolute)—the time taken to reach 115° C. was consistently about one min. In 12 experiments records were also kept of the time taken for the temperature to reach 126° C. Here again, with a high initial vacuum, 126° C. was reached almost instantaneously, but with low degrees of initial vacuum the points were again scattered, and in some cases the time taken for the temperature to rise from 115 to 126° C. was half an hour or more.

Six experiments were done with the autoclave packed as full as possible with six drums standing on their bases, rolls of cotton-wool, bowls, and utensils so as to fill the chamber completely. 100% of the test envelopes placed at random throughout the load were sterilized after 10 minutes' exposure to steam at 20 lb./sq. in. (1.4 kg./sq. cm.) when the initial pressure in the chamber had been reduced to 15 mm. Hg (absolute).

Discussion

The experiments here described have shown that, provided a high enough vacuum is drawn before steam is admitted, sterilizing temperatures can be reached inside a packed drum almost instantaneously, in spite of deliberate errors in loading. The exact level of vacuum required would be expected to vary with different experimental conditions. In the conditions we used, with a drum placed flat in the lower front position of the sterilizer, the initial vacuum required to ensure reliable penetration of steam was of the order of 20 mm. Hg (absolute). The temperature rose to 115° C. in about one minute and to 126° C. shortly afterwards. In experiments with lesser degrees of vacuum the times were much longer and less predictable. With downward displacement alone—that is, at an initial pressure of 760 mm. Hg (absolute)—it took around 40 minutes for the load to reach 115° C.

From these results it seemed likely that a tightly packed load could be rapidly sterilized if a high vacuum was first achieved. In six experiments carried out to test this hypothesis we found that complete sterility, judged by *B. stearothermophilus* spore strips and Browne's tubes, was achieved in 10 minutes at 20 lb./sq. in. (1.4 kg./sq. cm.) of steam after an initial vacuum of 15 mm. Hg (absolute).

Although a modern vacuum pump was fitted, the autoclave we used was over 10 years old and was not fitted with any other modern refinements. Even so, when the chamber was grossly overloaded the dressings could be sterilized and dried in a time totalling only 25 minutes from the closing to the opening of the door.

Our experiments have not answered, and were not meant to answer, the question whether preliminary vacuum or downward displacement is better as a method of removing air. It should be pointed out that in our experiments we deliberately used drums and loaded them incorrectly. The efficiency of downward displacement can probably be much increased if the chamber is correctly loaded and drums are not used. The decision on which method to use in new sterilizing plant can be made only after considering all the technical, financial, and administrative problems involved. For example, while a sufficiently high preliminary vacuum undoubtedly shortens the time taken for steam to penetrate and can probably safeguard against incorrect loading, the extra cost of an efficient pumping system may not be justified if the demands on the sterilizer are not excessive and if speed is not essential. However, if high vacuum equipment is to be fitted we believe our experiments show that it must be capable of reducing pressure in the chamber to at least 20 mm. Hg (absolute) in order to ensure consistent rapid sterilization.

Summary

A high vacuum system was used to remove air rapidly from an autoclave chamber before admitting steam. The time taken to reach a minimum sterilizing temperature of 115° C. inside a standard drum was found to be about one minute when the pressure in the chamber, before admitting steam, was reduced to 20 mm. Hg (absolute) or below. When lesser degrees of vacuum were used the times taken for the temperature to reach 115° C. were variable and prolonged.

It is suggested that if rapid and predictable sterilization is required in an autoclave fitted with a pump for drawing a preliminary vacuum then the pump should be capable of rapidly reducing the pressure in the chamber to 20 mm. Hg (absolute) or below.

We are indebted to Messrs. Edwards High Vacuum Ltd., Crawley, Sussex, for the loan of the pumping equipment and for valuable technical advice and assistance.

REFERENCES

Alder, V. G., and Gillespie, W. A. (1957). *J. clin. Path.*, **10**, 299.
Bowie, J. H. (1957). *Hospital Engineer*, **11**, 74.
Howie, J. W., and Timbury, M. C. (1956). *Lancet*, **2**, 669.
Perkins, J. J. (1956). *Principles and Methods of Sterilization*. Thomas, Springfield, Illinois.
Savage, R. Maxwell (1937). *Quart. J. Pharm.*, **10**, 445.

"As an example of 'the way emotion can disguise itself as opinion,' Sir WILLIAM HALEY described an incident drawn from his experience as a former director-general of the B.B.C. He told of a weekly index figure kept by the Corporation during the war, showing what listeners had thought of programmes as a whole, and of one week when the figure was so bad that a mistake was suspected. No mistake was found nor was there any difference in the programme that week. Looking for extraneous causes, the B.B.C. discovered that during the week in question, the failure of the paratroop drop on Arnhem had become fully known. This led them to compile a weekly graph of B.B.C. programme appreciation figures, related to the main events of the war. The B.B.C. also graphed a 'morale index' of the British nation. 'For all practical purposes,' Sir William Haley continued, 'the two graphs were a pair of tramway lines. Anything that made the public think the war was going better or worse automatically made them feel that their radio programmes had correspondingly improved or deteriorated. I have ever since been convinced that while public polls can tell us with remarkable accuracy what people think, they give us, as at present generally conducted and published, no clue as to why they think it.'"—*The Times*, March 12.

THE STIFF-MAN SYNDROME
PRELIMINARY REPORT OF A CASE

BY

T. M. L. PRICE, M.D., M.R.C.P.
Physician, Lewisham Hospital, London

AND

E. N. ALLOTT, D.M., F.R.C.P., F.R.I.C.
Group Pathologist, Lewisham Hospital, London

The first report of the stiff-man syndrome in this country, by Asher (1958), has aroused great interest, and prompts this preliminary account of a further case. So far no suggestions have been made regarding the aetiology of this strange condition: in the present case investigations are proceeding along several different lines, including detailed electromyographic studies by Dr. P. Bauwens at St. Thomas's Hospital and further work elaborating the biochemical findings described in this paper.

Publication at this stage will add to the very limited knowledge of the clinical appearances of the syndrome.

It was first described and named by Moersch and Woltman (1956) at the Mayo Clinic, and consists of a relentlessly progressive stiffness of muscles in the limbs and trunk interspersed with painful spasms in the affected groups, which may be of very great severity. So far it has not been amenable to any form of treatment. The overall picture is not reminiscent of any known disease, although the attacks do resemble and are equivalent in severity to the muscle spasms seen in tetanus.

Case Report

This case, that of Mr. L. L., aged 35, was mentioned briefly by Campbell (1958). His illness started in May, 1955, with sudden dislocation of his left thumb at the metacarpophalangeal joint while changing gear in driving his car. Because of subsequent pain in the hand and recurrent dislocation at frequent intervals, an open operation on the joint was performed two months later. Eight days after this he suddenly developed widespread, very painful muscle spasms and was admitted to hospital, where a diagnosis of tetanus was made; his trunk and all four limbs were involved, but there was no lockjaw.

He recovered quickly and was well enough to leave hospital after a fortnight. Subsequent dislocation of his thumb led to a second operation in February, 1956. From the beginning of 1956 onwards he developed recurrent painful muscular spasms in various parts of the body which have followed a clear-cut pattern and are now the main feature of his complaint.

Each attack starts suddenly at any time of the day or night, and the calves of the legs are usually the parts most severely affected. There may also be stiffness and spasm above the knees, in the buttocks and lower part of the back, and across the chest, but these cramps are not of comparable severity. The left forearm and hand are also frequently involved and there is often associated retention of urine. Occasionally the right arm is affected, and, rarely, a ptosis of the left eye occurs.

The attacks, particularly so far as the legs are concerned, are appallingly painful, and it is indeed difficult to describe them adequately. He states that he feels as though giants have taken each foot and leg and are tearing open the dorsum of the ankle-joint by forcible plantar flexion: watching him one can well imagine that this description is not exaggerated. The attacks last for anything from a few hours to several days and the painful spasms are continuous during