to the rays. I think that there are better methods of keeping bacteria out of wounds.

The Americans have been using ultra-violet rays for air sterilization for many years. It is a standard equipment in many schools and hospitals. Wells calculates that it is equivalent to 500 turnovers of air per hour, compared with the 25 turnovers by the best ventilation. In groups of schools the incidence of susceptibility to measles in an epidemic was from 9 to 15.5% in irradiated schools, and 55.3% and 51.8% in two unirradiated schools. Similar results have been found with chicken-pox. Experimentally, rabbits have been protected against air-borne tuberculosis. In my opinion ultra-violet light is the simplest and most efficient technique of this kind, and has no objectionable features if the eyes and skin are not irradiated.

Respiratory disorders, from tuberculosis and pneumonia, through sinusitis to the common cold, are far the most frequent of the diseases of mankind, and they are spread mainly through the air. The common infectious and virus diseases of childhood cause a high mortality and lifelong respiratory tract disease, and the air is again the commonest vehicle. Air-borne sepsis and cross-infection are common, particularly in wartime. There is still a tendency to laugh away the protagonists of the control of air-borne infection as faddists I heard a gynaecologist quite recently become vastly humorous at the suggestion that a nurse with a cold was a menace. But there is far too much hospital-bred infection, and far too many "sterile" operations go wrong. I feel quite sure that the time will come when the methods of controlling air-borne sepsis discovered in Europe and developed in America will return fully fledged to roost in their parent country.

BIBLIOGRAPHY

Andrewes, C. H., *et al.* (1940). *Lancet*, **2**, 770.
Bourdillon, R. B., Lidwell, O. M., and Thomas, J. C. (1941). *J. Hyg.*, Camb., **41**, 197.
—— —— and Lovelock, J. E. (1942). *British Medical Journal*, **1**, 42.
Colebrook, D. C. (1935). Med. Res. Cncl. Sp. Rep. Ser., No. 205. London.
van den Ende, M., *et al.* (1940). *Lancet*, **2**, 133.
—— and Spooner, E. T. C. (1941). Ibid., **1**, 751.
Flügge, C. (1897). *Z. Hyg.*, **25**, 179.
Trillat, M. A. (1938). *Ann. Hyg. publ.*, Paris, **16**, 49.
Twort, C. C., *et al.* (1940). *J. Hyg.*, Camb., **40**, 253.
Wells, W. F., and Wells, M. W. (1936). *J. Amer. med. Ass.*, **107**, 1698, 1805.

At a meeting of the North of England Obstetrical and Gynaecological Society held in Liverpool on July 4 Prof. T. N. A. JEFFCOATE described a simple method of replacing the retroverted uterus by manipulating it with a Hodge pessary. This method made the usual bimanual replacement unnecessary before inserting the pessary. With the patient in the left lateral position the Hodge pessary was inserted and allowed to take up its own position. The upper rim came to lie in the anterior fornix and the lower bar projected beyond the introitus. One finger was then inserted behind the lower bar, through the pessary, and in front of the upper rim, which was pushed against the anterior aspect of the cervix. The cervix was thus deflected backwards and the body began to rotate forwards. Ultimately the upper rim slipped past the cervix into the posterior fornix. By this time the retroversion was nearly always corrected but sometimes only partially, the uterus lying with its axis vertical. In such cases the upper end of the pessary was pushed firmly against the posterior vaginal wall and the posterior fornix repeatedly "stroked" backwards and slightly downwards with the pessary. At the same time the lower end of the pessary came to lie at a higher level. Thus the cervix was levered backwards and the fundus came forwards and the pessary was automatically left in its correct position. Prof. Jeffcoate also read a paper on pyrexia as a sign of endometriosis. He had found no reference to this sign in the literature but did not claim it as original. He said it had been established that temperature varied with the menstrual cycle, but the peak occurred premenstrually and the onset of the flow was characterized by a fall. In endometriosis he had several records of cases where a temperature up to 101° or 102° F. (38.3°-38.9° C.) appeared cyclically during menstruation and gradually disappeared one or two days after the flow ceased.

BRITISH ANTI-LEWISITE

A Report on its Use and Therapeutic Value in Arsenical Intoxications, from the BAL Conference, Medical Research Council

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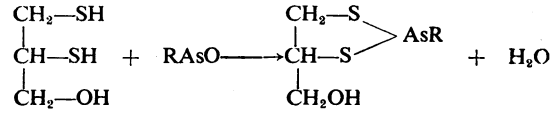
British anti-lewisite (BAL) is the name given to a compound, 2,3-dimercaptopropanol, discovered early in the war as a result of a planned research for the Ministry of Supply and developed as an antidote to the local and systemic damage caused by contamination of the skin or eyes with arsenical vesicant gases.

In the pure state it is a colourless oil, readily soluble in fat solvents, and soluble to the extent of about 6% in water. During 1941–2 its value in counteracting the effects produced by contamination with lewisite was exhaustively studied, and it was finally adopted officially as a suitable agent for the treatment of the effects of lewisite and the other arsenical vesicants. Its efficacy as an arsenical antidote and its power to reverse the tissue damage caused by arsenicals depend on its ability to form relatively stable ring compounds with arsenoxides, thereby diminishing the reaction of the arsenical with the tissues and increasing its urinary excretion from the system:



A review of the original work with lewisite has already appeared (Peters, Stocken, and Thompson, 1945), together with an account of the early developments of this work in the U.S.A. (Waters and Stock, 1945).

The application of BAL to the treatment of dermatitis and other complications arising in the course of arsenotherapy has also been extensively studied both in this country and in the U.S.A. The present short report summarizes the findings of a clinical trial of the therapeutic value of the compound carried out recently under the auspices of the Medical Research Council, a full account of which will shortly be published (Carleton, Peters, and Thompson: in the press).

Trial in Arsenical Dermatitis

The trial was based on the results obtained in 44 cases of arsenical dermatitis collected with the assistance of the Service Departments and the Ministry of Health. To facilitate the interpretation of any effects noted, the cases were selected so that the dermatitis was in each instance severe and widespread, 41 of them being of the acute exfoliative type.

Treatment was carried out by the clinicians in charge of the cases according to a scheme prepared by the BAL Conference, which was intended for initial guidance as to dosage. The ampoules of BAL used in this work were prepared by a modification of the method described by Eagle in the U.S.A., and contained 5% BAL in arachis oil

and benzyl benzoate; they were nitrogen-filled, and were sterilized by heating for one hour at 170° C.

The BAL was given by deep intramuscular injection into the thigh or gluteal region. In the hope of maintaining a concentration of the drug the following course of injections for adults of average weight was given in most cases: First day—4 injections of 2 ml. 5% BAL at 4-hourly intervals; second, third, and fourth days—2 ml. twice daily; fifth and sixth days—2 ml. daily. Where possible other local treatment of the affected skin was withheld.

From the reports received from the clinicians who co-operated in this trial it has been concluded that BAL therapy is of definite value in the treatment of this condition. Thirty-one of the 44 cases studied (70%) were benefited by the treatment, 23 of them (52%) strikingly so. The mean duration from the first injection of BAL to the time when healing was complete or nearly complete was 21 days. The earliest sign of response to treatment was in many cases a marked subsidence of the oedema present in the skin. In several instances clinical evidence of relapse was seen shortly after the end of the course of BAL therapy. In every case, however, this responded satisfactorily to a further short course of injections.

The outcome of this trial is in agreement with the results obtained elsewhere. The earliest use of BAL in the treatment of widespread arsenical lesions in man was in 7 cases of dermatitis (Longcope, Luetscher, Wintrobe, and Jäger, 1946) occurring in workers exposed to diphenylamine chlorarsine (phenarsazine chloride). These workers have also described 15 cases of generalized exfoliative dermatitis following the use of antisyphilitic arsenical drugs, and have stated that symptomatic and objective improvement regularly followed the administration of BAL. In this country Carleton *et al.* (1946), in an earlier series of 30 cases, have reported a beneficial effect in approximately 50% of cases.

Although favourable reports on the use of BAL in cases of arsenical encephalopathy and granulocytopenia have appeared in America (Report of the Council on Pharmacy and Chemistry of the American Medical Association, 1946; Eagle and Magnuson, 1946), we have not been able to study a sufficient number of cases of either of these conditions in this country to warrant a conclusion.

Clinical reports on the use of BAL in acute mercury poisoning (Longcope and Luetscher, 1946) and in gold intoxication (Cohen, Goldman, and Dubbs, 1947; Ragan and Boots, 1947; Lockie, Norcross, and George, 1947) have also been published, and the results obtained with these metals have been favourable. In the case of mercury 22 of the 23 patients studied recovered completely, although the amounts of mercury swallowed varied from 0.5 to 20 g., while 9 of the 10 cases of gold dermatitis described appear to have shown a prompt response to therapy. Work with lead, bismuth, and other metals has not yet progressed beyond the stage of animal experimentation.

Toxicity of BAL

As regards toxicity, the minimal dose given by intramuscular injection to man which causes toxic reactions lies between 3 and 5 mg./kg. Single doses of up to 8 mg./kg. have been given to normal subjects, and even at this level the toxic manifestations are completely reversible, lasting only a few hours. Apart from subjective phenomena, lacrimation, salivation, vomiting, and an elevation of both systolic and diastolic pressure occurred with these higher doses (Sulzberger, Baer, and Kanof, 1946; Modell, Gold, and McKeen Cattell, 1946). It should be pointed out that the therapeutic dose used in this country has been only about 1.5 mg./kg.; in America, on the other hand, a 10% solution of BAL has been used, and 6 doses at 4-hourly intervals of 3 mg./kg. have been given on the first day in severe cases (Eagle, 1946). In the treatment of acute mercury poisoning initial doses of up to 7 mg./kg. have been employed.

Though no evidence has been obtained of any increase in toxicity when BAL is injected into animals with experimentally induced renal damage, or of renal irritation in any of the cases in this series, increased toxic effects were present in animals with hepatic damage, which suggests that care should be exercised in the administration of BAL to patients with impaired liver function (Cameron, Burgess, and Trenwith, 1947). It should be added that BAL is not generally indicated in the treatment of post-arsphenamine hepatitis, the immediate cause of which appears to be infective in most cases (Salaman, King, Williams, and Nicol, 1944). Local abscesses have developed at the injection sites in a number of cases treated in this country. These may have been due to the septic condition of the skin in patients with exfoliative dermatitis of some standing, who are, in any case, prone to intercurrent infections of all kinds. This complication is probably preventable by the administration of BAL early in the course of the condition. A possible contributory factor is leakage of the substance into the subcutaneous tissue, which may be prevented by giving all the injections deep into the muscles. The abscesses, though troublesome, have healed satisfactorily with simple treatment, and do not, in our opinion, constitute a contra-indication to the use of BAL in such cases.

Conclusion

Up to the present time BAL has been manufactured by the Ministry of Supply, and in order that its therapeutic value could be firmly assessed distribution has been effected only through the Medical Research Council. It is considered that the value of the compound has now been established, and arrangements are being made by the Ministry of Supply for the preparation and issue of ampoules of BAL by firms in a position to exercise adequate biological control.

We would like to express our thanks to Miss F. B. Uffelmann, Ministry of Supply, and to the various clinicians who have co-operated in this trial, and also to Messrs. Boots Pure Drug Co., Ltd., and Messrs. Burroughs Wellcome and Co., Ltd., for the dispensing of the material used.

References

Cameron, G. R., Burgess, F., and Trenwith, V. S. (1947). *Brit. J. Pharmacol.*, **2**, 59.
Carleton, A. B., Peters, R. A., Stocken, L. A., Thompson, R. H. S., Williams, D. I., Storey, I. D. E., Levvy, G. A., and Chance, A. C. (1946). *J. clin. Invest.*, **25**, 497.
—— —— and Thompson, R. H. S. *Quart. J. Med.* In press.
Cohen, A., Goldman, J., and Dubbs, A. W. (1947). *J. Amer. med. Ass.*, **133**, 749.
Council on Pharmacy and Chemistry of the American Medical Association (1946). Ibid., **131**, 824.
Eagle, H. (1946). *J. vener. Dis. Inform.*, **27**, 114.
—— and Magnuson, H. J. (1946). *Amer. J. Syph. Gon. V. D.*, **30**, 420.
Lockie, L. M., Norcross, B. M., and George, C. W. (1947). *J. Amer. med. Ass.*, **133**, 754.
Longcope, W. T., and Luetscher, J. A. (1946). *J. clin. Invest.*, **25**, 557.
—— —— Wintrobe, M. M., and Jäger, V. (1946). Ibid., **25**, 528.
Modell, W., Gold, H., and Cattell, McKeen (1946). Ibid., **25**, 480.
Peters, R. A., Stocken, L. A., and Thompson, R. H. S. (1945). *Nature*, **156**, 616.
Ragan, C., and Boots, R. H. (1947). *J. Amer. med. Ass.*, **133**, 752.
Salaman, M. H., King, A. J., Williams, D. I., and Nicol, C. S. (1944). *Lancet*, **2**, 7.
Sulzberger, M. B., Baer, R. L., and Kanof, A. (1946). *J. clin. Invest.*, **25**, 474.
Waters, L. L., and Stock, C. (1945). *Science*, **102**, 601.

Further detailed reports of biochemical, pharmacological, and clinical aspects of the work on BAL may be found in: *Biochem. J.*, 1946, vol. 40; *J. Pharmacol.*, 1946, vol. 87 (Suppl.); *J. clin. Invest.*, 1946, vol. 25.