Summary

The subjects studied in this investigation were 100 healthy students and laboratory workers, 71 patients with disease of the liver, and 62 patients suffering from other diseases. Every care was taken to establish the clinical diagnosis beyond doubt.

The laboratory tests in all cases included estimations of the bilirubin, phosphatase, albumin, and globulin in the plasma, and measurement of the hippuric acid excretion and laevulose tolerance.

Analysis of the results indicates that a combination of data of this type has considerable diagnostic and prognostic value.

Changes in the plasma proteins in disease of the liver are of great significance. In cases of hepatitis with jaundice there is a close correlation between the time the jaundice has been present, the changes in the albumin-globulin ratio, and the prognosis. Irreparable liver damage has probably occurred if jaundice persists for more than two months or the plasma albumin falls below 2 g. %. In such cases the plasma globulin is usually over 4 g. %.

Estimation of the amount of bilirubin, phosphatase, albumin, and globulin in the plasma from a single blood specimen usually provides as much diagnostic and prognostic information as can be obtained from more elaborate tests of liver function.

Full case reports with protocols of the biochemical tests can be obtained from the authors.

We are indebted to the honorary staff of the Radcliffe Infirmary for permission to study their cases, and to Dr. A. H. T. Robb-Smith for doing the necropsies. All the laparoscopies were performed by Dr. A. M. Cooke. Miss M. Stanier, Mr. L. A. Rawlings, and Mr. E. R. Flack helped with the biochemical estimations.

REFERENCES

- Higgins, G., Macintosh, R. R., and O'Brien, J. R. P. (1942). Communication to Physiol. Soc., July, unpublished.
 — and O'Brien, J. R. P. (1944). In the press.
 — and Stewart, A. (1942). Communication to Physiol. Soc., July, unpublished.
 Howe, P. E. (1921). *J. biol. Chem.*, **49**, 109.
 King, E. J., and Armstrong, A. R. (1934). *Canad. med. Ass. J.*, **31**, 376.
 O'Brien, J. R. P. (1944). In the press.
 Probst, J. G., and Londe, S. (1940). *Ann. Surg.*, **111**, 230.
 Thannhauser, S. J., and Andersen, E. (1921). *Dtsch. Arch. klin. Med.*, **137**, 179.

SOME USES FOR DRY COLD THERAPY, AND A PROPOSED COOLING CABINET

BY

W. G. BIGELOW

Capt., R.C.A.M.C.

(A Canadian Casualty Clearing Station)

AND

E. C. G. LANYON

Capt., R.E.

(Army Blood Transfusion Service)

The therapeutic use of cold has lately been attracting the attention of investigators in many different fields. Recent studies point to the possibility of its much wider employment as a form of treatment in the future. In amputations for diabetic gangrene Allen (1941) and Bancroft *et al.* (1942) have shown the value of refrigeration as an anaesthetic and demonstrated how it appears to eliminate surgical shock from such a procedure. Its use in retarding the growth and relieving the symptoms of certain malignant tumours was investigated a few years ago by Temple Fay. Several other uses for dry cooling and actual freezing are being studied at the present time.

More important to military surgeons, however, is the steady accumulation of evidence for the value of cold treatment or controlled thawing of lesions of the extremities due to frost-bite and immersion in cold water (Webster *et al.*, 1942; Greene, 1941, 1942; Ungley, 1943). No attempt will be made to summarize that evidence here. Our purpose is to propose a cooling cabinet for the treatment of such lesions and to encourage the investigation of this form of treatment in three other types of cases: (1) wounds of the extremities which have impaired the blood supply sufficiently to endanger the limb; (2) traumatic arterial spasm; (3) peripheral embolism. The refrigerating unit is specially designed for treating such lesions of the extremities in the field. It is a relatively simple mobile

self-contained unit, not dependent on any cooling material that may be difficult to obtain. Observations made on a working model already constructed show that the temperature in the limb cabinet is easily controlled and can be maintained at any desired level.

Frost-bite and Immersion Foot

Greene (1941), by enumerating high casualty rates in previous military campaigns, has pointed out the serious potential danger of frost-bite in troops operating in cold weather. To quote one instance, he refers to the week ending Dec. 16, 1916, in which 3,104 frost-bitten men were admitted to medical units in the British Army alone. Adequate prophylaxis will prevent most cases of frost-bite, but tactical situations will not always allow the adoption of proper preventive measures, particularly in sudden changes of weather.

The rationale for the cold treatment of frost-bite and that for immersion foot are basically the same. Each is an attempt to reduce cell metabolism until such time as oxygen can be made available to the cell by the blood in sufficient quantity to satisfy the cell requirements at body temperature. In this way an oxygen deficit which would ordinarily cause death of the cell and gangrene of all or part of the extremity is avoided during the time taken for return to normal circulation and cell nutrition in the affected limb.

Webster first used and demonstrated clinically the value of local refrigeration of limbs in immersion foot. Under this treatment pain was relieved, the oedema subsided, blisters disappeared, and impending gangrene was arrested. During the period of exposure there is a vasoconstrictive ischaemia. On removing the limb from cold water and allowing it to thaw he describes a rapid increase in swelling, with pain. This is considered essentially a vascular response to tissue injury in which a liberated H-substance (Lewis, 1941) produces increased permeability of small vessels with resultant transudation into the tissues. Associated with this swelling there is an intense hyperaemia with anaesthesia and anhidrosis lasting several weeks, which, together with a sensitivity to adrenaline in the affected limbs, is evidence of a sympathetic-nerve or vasomotor paralysis (Ungley and Blackwood, 1942; Webster *et al.*, 1942). After the eighth to tenth day paraesthesias develop with later attacks of hyperhidrosis and cold-sensitiveness suggesting a Raynaud's phenomenon (Ungley).

Webster observes that "at the present it is not known how much of the fluid loss from vessels is due to actual damage of the vascular wall and how much is due to loss of neurogenic control of the vessels." The oxygen deficit in these cases he believes is caused by the intense tissue oedema hindering the transfer of oxygen to the cells plus the increased metabolic demand due to the reaction to tissue injury.

Frost-bite, a more serious problem in mobile war, is a condition in which actual freezing of tissues has occurred comparatively rapidly. Here one finds essentially the same pathogenesis, with a few possible differences depending for the most part on the rate of freezing. The swelling is usually not so pronounced. The period of reactive hyperaemia with increased swelling and pain following removal from cold has been personally observed in a few cases to last only a matter of minutes or hours (as compared with several weeks in immersion foot), depending on the severity of the lesions. This is possibly due to a lesser degree of tissue and nerve damage from a shorter period of exposure to thermal injury. Following this transient hyperaemia one sees the early onset of paraesthesia extending up the limb with varying degrees of sweating. A condition of "stasis" or capillary blockage by cells has been observed experimentally by Kreyburg and Rotnes (1932), confirmed by Greene, using a rapid-freezing technique which further increases the anoxia or oxygen deficit in the tissues. (Review of evidence: Bigelow, 1942.)

Thus, as in immersion foot, refrigeration by dry cooling will lower the metabolic demands of the part until normal neurovascular conditions have been re-established.

Webster in treating immersion foot has already used (1) cold air from a fan, (2) ice packs, (3) a cabinet for the feet in which the cooling device is air blown over ice by a fan. Greene (1942) for the treatment of frost-bite has recently devised a cabinet which is cooled by solid carbon dioxide

placed in an upper compartment with connecting flues. Ungley (1943) has lately constructed and used a similar refrigerator.

If the rationale of this treatment be accepted, frost-bite casualties on arrival at a C.C.S. or base medical unit should have the affected limbs inserted in a cooling cabinet, where they would remain until the circulation had been re-established and the greater part of the oedema had disappeared. During this period the temperature of the cabinet could be gradually increased daily until it reached room temperature. The length of time required for this "controlled thawing" would be several days, depending on the severity of the lesion.

Extremity Wounds, with Impaired Blood Supply

In an extremity in which the wound or injury has impaired the blood supply sufficiently to produce a danger of ischaemic gangrene one has a fundamentally similar problem. The ischaemia which is responsible for the oxygen deficit in the tissues may be due to ligation of main arteries, destruction of collateral branches, or intense swelling and oedema exerting pressure in fascial compartments and hindering the normal transfer of oxygen to the tissues.

To refrigerate the distal extremity of limbs with dangerously impaired blood supply, from whatever cause, appears perfectly reasonable. By so doing one lowers the metabolic requirements of the endangered tissues until such time as the collateral circulation has been established and swelling has subsided. It has been proved experimentally (Brooks and Duncan, 1940; Allen, 1941) that the ischaemic limb or tail of an animal survives a great deal longer when treated by dry cold than when left at room temperature. Allen also observes that the cold apparently inhibits blood-clotting and thrombosis, and he has demonstrated clinically that it prevents the coagulation of exudate in wound margins, thus facilitating drainage while retarding healing. Further benefits from cold therapy would be the relief from pain and the inhibition of any infective process that may be present in the affected part until such time as an improved blood supply might deal with it more effectively.

It may be argued that cold applied to the limb will induce a degree of arterial spasm and thus hinder the development of a collateral circulation. Very low temperatures, however, need not be used, and any tendency to vasospasm could be offset by coincident anaesthesia of the sympathetic nerve supply, heat applied to the other limbs, or vasodilator drugs. It is also possible that some phase of the biochemical process of tissue oxidation may be inhibited by too low a temperature, and in such an instance cold therapy could conceivably be harmful. If this is the case some form of temperature regulation is necessary.

The above experimental and clinical observations, based on apparently sound theory, should warrant investigation into the treatment of limb extremities, in certain types of wounds, by dry cooling and a gradual return to room temperature.

Traumatic Arterial Spasm

Increasing attention has been paid by surgeons recently to the occurrence of an arterial spasm associated with some wounds and fractures of the extremities (Cohen, 1940; Griffiths, 1940; Barnes and Trueta, 1942; MacFarlane, 1942). In such cases there is a history of trauma to the artery, which on exposure may or may not reveal any obvious evidence of damage. The resultant spasm has been shown experimentally (Barnes and Trueta, 1942) and clinically by these investigators to involve in most cases the entire vascular tree of the limb, and leads sometimes to gangrene. Griffiths has recently concluded that Volkmann's ischaemic contracture "is due to arterial injury and to the accompanying spasm of the arterial circulation." The pathology of the muscle necrosis in this condition and so-called traumatic arterial spasm has been observed to be similar (MacFarlane, 1942).

Cold therapy has already been considered and used by Canadian Army surgeons for traumatic arterial spasm. Again it must be remembered that cold in itself produces certain degrees of arterial spasm, and only further investigation will prove that in the balance greater benefit is conferred by its ability to lower the metabolic requirements of the tissues.

Acting on this latter assumption, however, these limbs can be refrigerated as an adjunct to the specific forms of therapy already recommended, such as surgical exposure of the artery, sympathectomy, arteriectomy, and the use of vasodilators. Since it has been observed that this spasm sometimes disappears spontaneously after a few days with the return of arterial pulse, cold therapy could be used as part of the conservation therapy routine provided no undue compression of the artery is considered likely to exist.

Peripheral Embolism

Acting on the same principle, and already suggested by Allen, dry cooling of a limb in which there has been an embolic blockage of its blood supply would enable the tissues to carry on at a reduced metabolic rate until the establishment of an improved circulation. Whether in conjunction with embolectomy or other lines of conservative treatment, tissue vitality would theoretically be retained during the time required for relief of the associated vasospasm or the development of a collateral circulation.

Description of Unit

The unit (Figs. 1-3) has been designed to accommodate two limbs if necessary. The cabinet or limb unit is cooled by cold brine, which circulates through coils in the wall, the

FIG. 1.—Side view of limb cabinet. *a*, Front panel with frame and slings attached. *b*, Studs for securing front panel. *c*, Trough with drain for condensate. *d*, Castors on front of frame. *e*, Guide for castors. *f*, Cork insulation. *g*, Brine pipes soldered to inner walls. *h*, Brine return pipe. *i*, Thermometer bulb. *j*, Thermometer dial. *k*, Canvas sleeve. *l*, Holes in front panel for entry of limbs. *m*, Brine-flow regulating valve. *n*, Hose union for brine pipe from reservoir.

FIG. 2.—Perspective of limb cabinet, showing one canvas sling. (For explanation of lettering see Fig. 1.)

temperature of the cabinet being regulated by merely adjusting the rate of flow of cold brine, using a stopcock and thermometer, conveniently placed for the patient to do his own adjusting.* The slings for the limbs are suspended from

* This method was used satisfactorily on the experimental model, but it has since been determined that it would be possible to have an automatic valve made which would pass just the requisite amount of brine to maintain the cabinet at any predetermined temperature. The whole equipment would thus be independent of any manual control.

a metal framework which is integral with the front panel. Thus by detaching the front panel the limbs can be withdrawn for observation or dressings with a minimum of trauma and without disturbing their position in the slings. This operation is facilitated by the provision of castors on the far end of the frame running in guides on the floor of the cabinet.

The brine circulating in the limb cabinet is cooled in a reservoir to a predetermined temperature by a separate refrigerating machine and pumped to the limb cabinet through a flexible tube. Several limb cabinets can be attached to the brine supply at one time, thus allowing treatment of more than one patient, and by adjusting the stopcocks (previously described) on the limb cabinets it is possible, if necessary, to maintain different temperatures in each of the cabinets.

The actual refrigerating machine with brine reservoir would be a mobile unit mounted on a trolley and operated entirely by electricity. Its essential components would be a small compressor operated by an electric motor, an air-cooled condenser, and an automatic expansion valve for regulating the flow of refrigerant. The brine reservoir

vaporized would be pumped out by the compressor and recondensed in the air-cooled condenser. The brine could be kept within 2°C . of any desired temperature by means of a thermostat, which would automatically start and stop the electric motor driving the compressor. The cooled brine would be taken from the reservoir by a small electrically driven centrifugal pump, and circulated to the various units by way of a manifold and flexible hoses, returning afterwards to the reservoir for re-cooling. It is estimated that the dimensions of a complete refrigerating unit as described, and capable of operating up to four limb cabinets, would not exceed 2 ft. 6 in. by 2 ft. 6 in. by 2 ft. 3 in.

The cabinet described can be operated over a very wide range of temperature. It has been determined experimentally that in order to maintain a cabinet temperature of 4°C . to 6°C . the brine circulating need only be 0°C . to -2°C . Therefore, by lowering the temperature of the brine reservoir, which is done by adjustment of a thermostat, temperatures well below freezing-point could be maintained in the cabinet.

The working model constructed by one of us (Lanyon) for investigation has a small limb cabinet capable of accommodating a hand and lower forearm (see photographs, Fig. 3). Observations made on an empty cabinet and again with a normal limb inserted proved the ability of the cabinet to assume any given temperature and to maintain this temperature with the minimum of adjustment. Dermatherm readings, to record the resultant changes in skin temperatures, made by attaching a thermocouple to the dorsum of the hand, showed coincident variation of skin temperatures (see Graph). With such an apparatus, cabinet temperatures from 4°C . to room temperature were obtained. After two hours' exposure at a cabinet temperature around 12°C . the limb appears to be completely chilled, evidence of this being the subjective numbness and the fact that it takes several hours for the skin temperature to return to normal after removal from the cabinet.

Summary

A description is given of a refrigerating device to investigate the dry cold treatment of frost-bite, traumatic arterial spasm, peripheral embolism, and certain wounds of the extremities.

Observations made on a working model have proved it capable of providing the conditions necessary for such treatment.

The apparatus is simple, portable, and flexible in operation, and has been designed primarily to meet the requirements of an army in the field.

We acknowledge with thanks the helpful advice of Lieut.-Col. E. H. Botterell, Basingstoke Neurological and Plastic Surgery Hospital, and the facilities provided by the Officer Commanding Army Blood Supply Depot for carrying out the experimental work.

REFERENCES

- Allen, F. M. (1941). *Amer. J. Surg.*, **52**, 225 (see Bibliography).
 Bancroft, F. W., Fuller, A. G., and Ruggiero, W. F. (1942). *Ann. Surg.*, **115**, 621.
 Barnes, J. M., and Trueta, J. (1942). *Brit. J. Surg.*, **30**, 74.
 Bigelow, W. G. (1942). *Canad. med. Ass. J.*, **47**, 529.
 Brooks, B., and Duncan, G. W. (1940). *Ann. Surg.*, **112**, 130.
 Cohen, S. M. (1940). *Guy's Hosp. Rep.*, **90**, 201.
 Greene, R. (1941). *Lancet*, **2**, 689.
 — (1942). *Ibid.*, **2**, 695.
 Griffiths, D. L. (1940). *Brit. J. Surg.*, **28**, 239.
 Kreyburg, L., and Rotnes, L. (1932). *Acta path. microbiol. scand.*, Supp., **11**, 162.
 Lewis, Sir T. (1941). *British Medical Journal*, **2**, 795.
 MacFarlane, J. A. (1942). *J. Bone Jt. Surg.*, **24**, 739.
 Ungley, C. C. (1943). *Lancet*, **1**, 681.
 — and Blackwood, W. (1942). *Ibid.*, **2**, 447.
 Webster, D. R., Woolhouse, F. M., and Johnston, J. L. (1942). *J. Bone Jt. Surg.*, **24**, 785.

FIG. 3.—The experimental cabinet. A, View of cabinet with front in position. B, Front removed, showing rest for hand. C, Patient's forearm in position. (The thermometers shown were used in making experimental observations.)

FIG. 4.—Graph showing record of cabinet and skin temperatures (June, 1943).

would be mounted alongside the machine, and would consist of an insulated tank with a suitable coil of cooling pipe immersed in the brine. This coil would be cooled by admission of liquid refrigerant through the expansion valve; the refrigerant when

A new decree has been issued in Rumania which states that every-one with venereal disease must undergo treatment, and premarital certification of freedom from infection is obligatory. Physicians must report defaulting patients. Persons exposed to risk through their profession—e.g., those serving in hotels, restaurants, night clubs, public baths, as well as pedlars and street vendors—are subject to periodic examinations. Correctional imprisonment of 1 to 3 years is imposed on clandestine prostitutes and proprietors of hotels who allow prostitution on their premises. Knowing transmission of the disease to others carries a sentence of 1 to 5 years' correctional imprisonment and a fine of 50,000 to 200,000 lei. . . . Persons undergoing medical treatment at the time of transmission of the disease will be severely punished without the application of extenuating circumstances. Free blood tests are made by the State. Brothels are again permitted by law.