- Fennel, E. A. (1919). *Abst. Bact.*, 3, 12.
 Griffiths, J. J. (1942). *Publ. Hlth Rep. (Wash.)*, 57, 707.
 — (1944a). *Ibid.*, 59, 1374.
 — (1944b). *Ibid.*, 59, 1516.
 Kraus, R., and Kovacs, N. (1928). *Z. Immun.-Forsch.*, 55, 316.
 — and Pribram, E. (1905). *Wien. klin. Wschr.*, 18, 999.
 Quoted by R. Pollitzer, *Cholera*, p. 147. W.H.O., Geneva, 1959.
 Mukerjee, S., and Guha Roy, U. K. (1962). *Brit. med. J.*, 1, 685.

- Ranta, L. E., and Dolman, C. E. (1943). *Canad. J. publ. Hlth.*, 34, 26.
 Takita, J. (1939). *Kitasato Arch. exp. Med.*, 16, 218. Quoted by R. Pollitzer, *Cholera*, p. 211. W.H.O., Geneva, 1959.
 Watanabe, Y., and Felsenfeld, O. (1961). *J. Bact.*, 82, 43.
 Wilson, G. S., and Miles, A. A. (1955). *Topley and Wilson's Principles of Bacteriology and Immunity*, 4th ed., p. 610. Arnold, London.
 W.H.O. (1959). *Wld Hlth Org. techn. Rep. Ser.*, No. 179.

APPARATUS FOR CONTINUOUS INFUSION CHEMOTHERAPY

BY

D. E. PEGG, M.B., B.S. R. E. TROTMAN, B.Sc., A.Inst.P. N. H. PIERCE, F.I.S.T.

From the Departments of Radiotherapy and Physics, Westminster Hospital, London

Following the original use of intra-arterial nitrogen mustard by Klopp *et al.* (1950), several workers have developed arterial infusion techniques for the treatment of localized malignant disease (Sullivan *et al.*, 1959; Horwitz, 1960; Westbury *et al.*, 1962; Espiner *et al.*, 1962). It has been found that with the most commonly used antimetabolite, methotrexate, optimum results are obtained after at least two weeks of continuous infusion. This necessitated the development of simple and reliable apparatus for intra-arterial infusion. The related technique of continuous intravenous infusion of alkylating agents (K. A. Newton, personal communication 1960) requires somewhat similar apparatus.

In most cases a pressure of 170 mm. Hg (90 in. H₂O) is adequate for intra-arterial infusion, and this can easily be provided by gravity feed. However, the drip-infusion technique has three main deficiencies. In the first place, practical considerations limit its use in hypertensive patients who may require infusion pressures as high as 350 mm. Hg (190 in. H₂O). Secondly, it is difficult to control the volume of fluid infused to less than 1,500 ml. a day with a conventional drip-chamber, and this may be excessive in children and patients with cardiac failure or impaired renal function. Finally, since the hydrostatic pressure is constant there is no increase in pressure during incipient blockage of the catheter or increased resistance due to movement by the patient. Consequently there are frequent varia-

tions in flow rate and complete cessation sometimes occurs.

It is possible to control the infusion at a lower rate by the use of the micro-drip chamber shown in Fig. 1. This consists of a Pasteur pipette (A) with a silicone

FIG. 1.—Micro-drip chamber.

rubber stopper (B) through which passes a 0.7-mm. hypodermic needle (C). With this simple refinement it is possible to control the infusion at a rate of approximately 500 ml. a day. The difficulties caused by variations in infusion rate have been alleviated by designing a drip-rate monitor and alarm. This device is operated by a special drip-chamber containing two platinum electrodes (Evans, 1955); each drop of fluid momentarily connects the electrodes, thus providing a signal to operate the monitor. The apparatus is driven by a 6-volt battery and provides visual indication of each drop. The drip rate is displayed on a meter calibrated from 0 to 50 drops a minute, and an alarm operates if the rate falls below 10 drops a minute for more than 1½ minutes.

These devices help considerably in the management of arterial drip infusions, but when the blood-pressure is so high as to preclude the use of this method or when

FIG. 2.—Arterial infusion pump.

it is desired to restrict the fluid intake still further, an arterial pump is essential. This technique has the additional advantages of providing a constant infusion rate and of overcoming fluctuations in pressure at the catheter tip. The apparatus we have designed incorporates several safety devices and is shown diagrammatically in Fig. 2. The infusion fluid is pumped from two bottles connected so that the second bottle does not begin to empty until the first bottle

bridge, for constructing the air-trap and electrode assembly. Mr. A. P. Evans, of Delta Technical Services Ltd., Kingston-on-Thames, developed the pressure-sensitive switch. The electrode drip-chambers and drip-rate monitor are obtainable from Electronic Machine Control Ltd., of Thornton Heath, Surrey, who can also supply the complete arterial pump equipment.

Financial support for this work was provided by Mr. Geoffrey Harmsworth, the British Empire Cancer Campaign, and the Board of Governors of Westminster Hospital. One

FIG. 3.—Automatic syringe.

is completely empty. The second bottle is suspended from a weight-sensitive switch which is set to operate if this bottle begins to empty. The pump itself is adapted from the proportioning pipette of Dr. I. D. P. Wooton, and is driven by an induction motor to give an output of 400 ml. a day. The output is fed to a pressure-sensitive switch which is set to operate at 100 mm. Hg above the patient's measured arterial pressure; this permits the pump to develop a moderate increase in pressure to overcome variations of flow resistance but stops it in the event of a complete blockage due to clotting or extravasation of the catheter tip. Finally, the fluid passes through an air-trap, and electrodes mounted in the top of this chamber actuate a relay if the amount of trapped air increases above a predetermined limit. The catheter connector incorporates a lateral Gordh cap to facilitate the injection of dyes used to locate the position of the catheter tip. In addition to the automatic safety switches already mentioned, failure of the mains supply, the pump motor, and some important circuit components are monitored; each safety device automatically stops the pump and switches on a single prominent warning lamp. Those parts of the apparatus which come into contact with the infusion fluid can be autoclaved except for the diaphragm of the pressure-sensitive switch; this is sterilized with 0.5% alcoholic domiphen bromide ("bradosol").

Automatic syringes have also been used for continuous infusion treatment of cancer. We have designed a simple instrument of this type which consists of a syringe, the plunger of which is driven from a screw thread rotated by a small synchronous motor. A quick-release coupling facilitates speedy resetting and a safety switch stops the motor and switches on a warning light when the plunger reaches the end of its traverse. Remote visual and/or audible warning of this event is provided. The apparatus is shown in Fig. 3; it is used to infuse cold acid solutions of alkylating agents into a dextrose-saline intravenous infusion close to the needle. This technique is designed to reduce decomposition of the drug during infusion. A very slow rate of infusion is required and a 10-ml. syringe driven by a 2 B.A. thread at 12 r.p.h. provides a flow rate of 2 ml./hour. Variations in drug-infusion rate can be obtained by varying the concentration of the solution.

We would like to thank Messrs. Metal Machinists Ltd., of London, and Mr. B. Cooper, of Cathodeon Ltd., Cam-

bridge, for constructing the air-trap and electrode assembly. Mr. A. P. Evans, of Delta Technical Services Ltd., Kingston-on-Thames, developed the pressure-sensitive switch. The electrode drip-chambers and drip-rate monitor are obtainable from Electronic Machine Control Ltd., of Thornton Heath, Surrey, who can also supply the complete arterial pump equipment.

REFERENCES

- Espiner, H. J., Vowles, K. D. J., and Milnes Walker, R. (1962). *Lancet*, **1**, 177.
 Evans, F. (1955). *Ibid.*, **1**, 29.
 Horwitz, H. (1960). *Brit. J. Radiol.*, **33**, 679.
 Klopp, C. T., Alford, T. C., Bateman, J., Berry, G. N., and Winship, T. (1950). *Ann. Surg.*, **132**, 811.
 Sullivan, R. D., Miller, E., and Sikes, M. P. (1959). *Cancer (Philad.)*, **12**, 1248.
 Westbury, G., Newton, K. A., Humble, J. G., Ford, H. T., Pegg, D. E., and White, W. F. (1962). *Brit. med. J.*, **1**, 1238.

Preliminary Communications

Development of Kala-azar in Man after Inoculation with a *Leishmania* from a Kenya Sandfly

The isolation of a strain of *Leishmania* in Kenya from a sandfly presumed to be *Phlebotomus martini* has been recorded by Heisch, Wijers, and Minter (1962). The specimen was collected on June 10, 1961, from a termite hill in the Tseikuru location of Kitui district, where many Africans have been infected with kala-azar during the past 10 years.

The flagellates which were in the anterior part of the midgut of the sandfly were inoculated into a hamster; this was sacrificed about six months later (December 20) and found to be heavily infected. The strain has since been maintained in N.N.N. medium.

As the identity of the sandfly strain was uncertain, it was decided to test its pathogenicity in man. Cultures of the strain were inoculated intradermally and subcutaneously into the right forearms of four volunteers on February 6, 1962. The volunteers who took part in this study were told quite explicitly that the inoculation might produce kala-azar and that this was a serious disease. They were assured that if they developed kala-azar they would be diagnosed promptly as a result of their weekly medical and pathological examinations; they were also assured that they would be admitted to hospital and treated fully as soon as diagnosis was established.

Three of the subjects had negative leishmanin tests (Manson-Bahr, 1961a), while the fourth had previously been immunized with a rodent strain of *Leishmania* (Manson-Bahr, 1959, 1961b) and was leishmanin-