BIBLIOGRAPHY

- Forrester, A. C., and Saunders, R. C. O., *Brit. J. Anaesth.*, 1955, 27, 594.
 Kinmonth, J. B., *Brit. med. J.*, 1952, 1, 59.
 ——— Hadfield, G. J., Connolly, J. E., Lee, R. H., and Amoroso, E. C., *Brit. J. Surg.*, 1956, 44, 164.
 ——— and Simeone, F. A., *ibid.*, 1952, 39, 333.
 ——— and Perlow, V., *Surgery*, 1949, 26, 452.

CLINICAL CASE REFERENCES

- Adams, R. C., *Intravenous Anesthesia*, 1944, p. 506. Paul B. Hoeber Inc., New York and London.
Brit. med. J., 1954, 1, 766.
 Cohen, S. M., *Lancet*, 1948, 2, 361, 409.
 Culbert, T. D., *Brit. med. J.*, 1954, 1, 393.
 Dundee, J. W., *ibid.*, 1953, 1, 402.
 Fell, J. N., *ibid.*, 1953, 1, 95.
 Hughes, D. C., personal communication, 1958.
 Lees, J., *Lancet*, 1943, 1, 788.
 Lundy, J. S., *Clinical Anesthesia*, 1942, p. 542. Saunders, Philadelphia and London.
 Richardson, W. W., *Brit. med. J.*, 1956, 2, 754.
 Rob, C. G., personal communication, 1957.
 Rollason, W. N., *Brit. med. J.*, 1950, 1, 1350.
 Stuart, P., *ibid.*, 1955, 2, 1308.
 Swerdlow, M., *ibid.*, 1954, 1, 258.

GANGRENE OF FOREARM AFTER INTRAMUSCULAR CHLORPROMAZINE

BY

R. J. HAMER HODGES, F.F.A.R.C.S., D.A.

Consultant Anaesthetist, Portsmouth Group Hospitals

Anaesthetists are aware of the catastrophes associated after the spread of accidental extravenous injection of piridossal-diethazine (Sénèque and Huguenard, 1953), 1955). Recently, similar tragedies have been reported with hydroxydione (Schwarzkopf, 1958), and also after the spread of accidental extravenous injection of piridosal-diethazine (Sénèque and Huguenard, 1953), and promazine (Opinsky *et al.*, 1958). Gangrene due to an intramuscular premedicant injection is a less-known hazard, and appears to have been unreported.

Case Report

A woman aged 52, with a history of constitutional psychotic instability, accidentally sustained severe third-degree burns covering approximately 35% of her total body surface from the waist downwards.

After skin-grafting, the patient relapsed into acute mania, which made treatment difficult. During psychotherapeutic therapy the burnt areas were treated in enveloping plaster and were re-dressed as necessary under light general anaesthesia. Sepsis and decubitus ulceration took place under the plaster jacket, resulting in toxæmia and signs of renal damage. Blood transfusions and strenuous general measures were continuously necessary to maintain her general condition. After five months of treatment the patient had improved mentally and was alert and sensible, but her physical state had slowly depreciated and she had not tolerated repeated anaesthesia well. The dressings were latterly performed under light basal sedation. On the second occasion 50 mg. of chlorpromazine was ordered by intramuscular injection. The patient's legs and buttocks were covered with healing burns, and previous intravenous and intramuscular therapy had left residual soreness in both arms.

The injection (2 ml. of 2.5% solution), which was administered by a trained staff nurse, was given into the anterior aspect of the right biceps area, this being considered to be the best available site. No complaint of pain or

discomfort was made by the patient at the time of injection, but twenty minutes later she remarked that her arm felt dead. On examination the arm was found to be flaccid, cold, and white. The brachial artery was pulsating in the upper arm, but from the site of injection downwards no circulation could be detected. From 1½ in. (3.8 cm.) above the elbow-joint to the finger-tips the limb appeared to be completely exsanguinated. Procaine (5%) was immediately infiltrated around the brachial artery at the injection level, and 25 mg. of tolazoline was administered intramuscularly. Neither measure had any obvious effect. Two and a half hours later a stellate ganglion and brachial plexus block was performed, using 1% lignocaine; this was followed after 15 minutes by Horner's syndrome, but by no alteration in the appearance of the arm. A few minutes later 40 mg. of papaverine in 20 ml. of water was injected into the subclavian artery, after which there appeared to be a slight flushing of the skin for an inch (2.5 cm.) or more below the previous line of exsanguination. Immediately after this procedure an intravenous injection of 15,000 units of heparin was given. Surgical exploration was undertaken eight hours from the time of the original intramuscular injection, the patient receiving light general anaesthesia with thiopentone, cyclopropane, nitrous oxide, and oxygen. The brachial artery, exposed in the upper arm, was found to be pulsating and healthy. At the level of the intramuscular injection there was some periarterial discoloration and haematoma formation, but no evidence that the artery had been punctured. From here downwards the vessel was contracted and immobile, and no blood could be aspirated therefrom. A 2% solution of papaverine was applied locally and 40 mg. of the drug in 20 ml. of water was injected into the artery at its lowermost normal point. These measures had no visible effect. Arteriotomy and arteriectomy were considered inadvisable.

Post-operatively, continuous heparinization was maintained and vasodilatation was encouraged by intramuscular tolazoline and by contralateral limb-heating. Support and gentle passive exercises were applied to the affected limb. In a few days there was a slight regression of the exsanguinated area on the radial side of the arm, and mottled bluish patches appeared around the surgical wound in the upper arm and spread into the forearm, particularly on the ventral aspect. The remainder of the forearm and hand remained bloodless, flaccid, and cold. Dry mummification took place in the finger-tips (Figs. 1 and 2). A line of separation eventually appeared, medially just below and laterally just above the elbow-joint. By the fifth day it was obvious that amputation of the forearm was inevitable, but in view of the patient's gradually depreciating condition conservative treatment was continued. The

FIG. 1.—Ventral aspect of arm eight days after an intramuscular injection of chlorpromazine.

FIG. 2.—Dorsal aspect of arm eight days after an intramuscular injection of chlorpromazine.

patient died in an uraemic coma following renal failure two weeks after the intramuscular injection and five and a half months after her original injuries.

Pathology

At necropsy dry gangrene of the right hand, forearm, and elbow was confirmed, the brachial artery being thrombosed from the mid-upper arm downwards. Histologically the artery was occluded by an unorganized red thrombus. There was no evidence of intimal proliferation, and the elastic laminae and media appeared normal. The vessel was incompletely surrounded by an organizing haematoma involving the adventitia.

The pathological condition of the arm was considered to be one of several associated causes of death, the primary cause being septicaemia after burns.

Discussion

Arterial spasm, with ischaemic tissue necrosis as a secondary manifestation of sciatic-nerve injury, has been reported after intramuscular therapy (Lee and Stallworth, 1958), but otherwise it would seem that nerve injuries (Turner, 1920; Schmuttermeyer, 1936; Medical Protection Society, personal communication, 1958; Cohen personal communication, 1958), transient arterial spasm or local necrosis only (Gammel, 1927; Schönbauer, 1955; Harper, personal communication, 1958; Dundee, personal communication, 1958) are the main complications after intramuscular injections.

Chlorpromazine causes pain and irritation after injection (Dripps *et al.*, 1955; Simpson, 1955; Dundee, 1957) associated with an apparent inflammatory reaction. Thrombophlebitis, sterile abscess formation, and sloughing may occur (Harper, personal communication, 1958) occasionally necessitating skin-grafting (Dundee, personal communication, 1958).

The systemic vasodilatory effects of chlorpromazine are well established. Foster *et al.* (1954) showed, further, that in conscious subjects chlorpromazine caused a local vasodilatation (in doses of 1/80–1/6 mg./min. added to a brachial-artery infusion of 4 ml./min.). This effect was thought to be due either to blockage of the sympathetic vasoconstrictor nerve impulses in the vessel wall or to a direct effect on the arterial muscle. It is more than unexpected, therefore, that in this instance the drug produced intense arterial spasm. The patient did not complain of any symptoms at the time of injection, and at operation there was no local evidence of arterial puncture. Therefore the assumption remains that the periarterial injection caused an intense local irritation and an intractable reflex local and peripheral arteriolar spasm. A similar irritant effect on an adjacent artery after an inadvertent perivenous injection resulted in gangrene of the limb after other phenothiazine derivatives, piridosal-diethazine (Sénèque and Huguenard, 1953), and promazine (Opinsky *et al.*, 1958). The condition appears to have some resemblance to that known to follow high-altitude frostbite (Davis *et al.*, 1943) and in some instances of misplaced thiopentone injections (Cohen, 1948). The appearance of the arm and the absence of oedema suggested that the circulation was completely arrested in the forearm and that the main digital arteries became thrombosed within a very short time. Thereafter all treatment was useless.

The only beneficial effect appeared to follow the early intra-arterial injection of papaverine. Lack of precedence and first-hand experience of such cases led

to some degree of reluctance to embark on surgical exploration, and this undoubtedly lessened the chances of success.

General anaesthesia of the type used is said to increase the peripheral circulation by 64%, but neither this nor the local operative measures applied resulted in any measurable effect in the limb.

It is impossible to dissociate completely the fatal outcome from the local condition of the limb. Renal and systemic effects from the adsorption of dead muscle have been shown to follow arterial thrombosis in the legs (Guthkelch, 1943; Bywaters and Stead, 1945), but in the absence of any effective circulation one would have expected these effects to be minimal.

While admitting that the choice of site and the technique of intramuscular injections are of major importance, there can be little argument that drugs with known irritant qualities should be administered in dilute solutions. Further, when no suitable muscle mass is available an alternative method of treatment should be instituted.

Summary

A unique case is reported in which the accidental periarterial intramuscular injection of chlorpromazine led to intractable local and peripheral arteriolar spasm, thrombosis, and eventual massive gangrene of the arm and forearm.

The particular considerations of the case are discussed.

REFERENCES

- Bywaters, E. G. L., and Stead, J. K. (1945). *Clin. Sci.*, **5**, 195.
Cohen, S. M. (1948). *Lancet*, **2**, 409.
Davis, L., Scarff, J. E., Rogers, N., and Dickinson, M. (1943). *Surg. Gynec. Obstet.*, **77**, 561.
Dripps, R. D., Vandam, L. D., Pierce, E. C., Oech, S. R., and Lurie, A. A. (1955). *Ann. Surg.*, **142**, 774.
Dundee, J. W. (1957). *Anaesthesia*, **12**, 215.
Forrester, A. C., and Saunders, R. C. O. (1955). *Brit. J. Anaesth.*, **27**, 594.
Foster, C. A., O'Mullane, E. J., Gaskell, P., and Churchill-Davidson, H. C. (1954). *Lancet*, **2**, 614.
Gammel, J. A. (1927). *J. Amer. med. Ass.*, **88**, 998.
Guthkelch, A. N. (1943). *Brit. med. J.*, **2**, 245.
Lee, W. H., jun., and Stallworth, J. M. (1958). *Angiology*, **9**, 63.
Opinsky, M., Serbin, A. F., and Rosenfeld, J. E. (1958). *J. Amer. med. Ass.*, **168**, 1224.
Schmuttermeyer, F. (1936). *Wien. klin. Wschr.*, **49**, 1197.
Schönbauer, L. (1955). *Wien. med. Wschr.*, **105**, 22.
Sénèque, J., and Huguenard, P. (1953). *Anésth. et Analg.*, **10**, 627.
Simpson, R. E. (1955). *Canad. Anaesth. Soc. J.*, **2**, 14.
Schwarzkopf, H. (1958). *Dtsch. med. Wschr.*, **83**, 1089.
Turner, G. G. (1920). *Lancet*, **2**, 819.

The New Zealand Cabinet has decided that, when a second medical school is built, it will be in Auckland. Mr. W. H. COCKER, chancellor of Auckland University, said he had been advised to this effect by the Prime Minister, Mr. WALTER NASH. No site has yet been decided on. The Senate of the New Zealand University appointed a committee in 1953 to recommend a site for a new medical school. It decided on Auckland, and since then it has been assumed that the school would be established there. But, because the Government had made no formal decision on the committee's recommendation, a deputation from Auckland University, including representatives of the Auckland Hospital Board, recently urged the Government to settle on Auckland as the site. The Senate has not fixed any date when the second medical school will be required (New Zealand Release No. A.19/59).