Case Reports

ERGOT POISONING

G. GLAZER, M.B., B.S.
House Surgeon, Surgical Unit.

K. A. MYERS, M.B.(Melb.), F.R.A.C.S.
Senior Registrar, Surgical Unit (Smith and Nephew Fellow).

E. R. DAVIES, M.B., M.R.C.P.E., F.F.R.
*Senior Registrar, Radiological Dept.,
St. Mary's Hospital, London, W.2.*

ERGOTAMINE tartrate is frequently prescribed for the treatment of migraine. Complications from the drug are rare but potentially serious.

A case is presented of severe lower limb arterial spasm due to ergotamine tartrate taken sublingually and orally for migraine. This case provided an opportunity to study the vascular and systemic effects of the drug and to review the literature concerning the risk, manifestations and treatment of ergot poisoning.

Case Report

Mr. E.K., a 33 year old van-driver, presented in September 1964 having suffered a sudden onset of severe intermittent claudication in both calves three days previously; this was associated with rest pain in both feet and a low lumbar backache. In 1961 he had experienced an identical acute attack; his symptoms had then improved gradually over six months although a variable degree of mild claudication had persisted. No precise diagnosis had been made and treatment had consisted of numerous vasodilator drugs which had little effect. During the past six months he had noticed post-prandial dyspepsia and had lost one and a half stone in weight.

Further questioning revealed that the patient had suffered from typical migraine since adolescence. The headaches were confined to the left eye and left side of the head, and were accompanied by fortification spectra and occasional vomiting. The headaches had been increasing in frequency and by September 1964 were occurring twice a week.

The patient had received various drugs for his migraine for many years. There is no record of treatment before 1959 but ergotamine preparations were probably prescribed. From 1959 to 1961 he had consistently taken two tablets per day of Lingraine, a sublingual preparation containing 2 mg. of ergotamine tartrate. From 1961 to 1964 documentation of treatment was incomplete, but ergotamine preparations were often taken. Prior to the recent exacerbation of claudication he had taken eleven tablets of Migril over a period of five days (each tablet containing 2 mg. of ergotamine tartrate, 100 mg. of caffeine and 50 mg. of cyclizine hydrochloride); the last tablet was taken on the day he developed acute claudication and two days later he was admitted to hospital.

On admission the oral temperature was 99.2°F., the pulse rate was 84 per minute and the blood pressure was 110/80 mm.Hg. in both arms. The pulses in the arms and neck were normal; the femoral pulses were weak and equal, but no pulses were palpable below these in either leg. There were no arterial bruits. The feet were white and cold, with anaesthesia of the toes but no evidence of gangrene. General examination revealed no other abnormality apart from constricted pupils. A provisional diagnosis was made of arteriospasm secondary to chronic overdosage of ergotamine tartrate.

Progress: Following admission the patient became drowsy, nauseated and suffered from attacks of vertigo. Five days after cessation of ergotamine therapy the foot pulses became palpable and he then developed intense burning sensations in both feet (St. Anthony's Fire).

It was considered that final confirmation of the diagnosis necessitated reproduction of the symptoms with a small provocative dose of ergotamine. One day after the return of the foot pulses, ergotamine tartrate was recommenced, and a total of 10 mg. was given orally over a period of three days; the foot pulses disappeared eighteen hours after the initial 2 mg. dose and reappeared forty eight hours after the drug was stopped. A further single oral dose of 2 mg. ergotamine tartrate given seven days later caused the foot pulses to disappear within twelve hours and reappear after a further twenty-four hours.

The patient was discharged from hospital three weeks after admission with palpable foot pulses and reduced pain. His other symptoms had also improved. One week later he developed a small haemorrhagic blister on the under surface of the right fifth toe but following incision this healed rapidly. Six weeks after discharge the claudication distance had increased to 400 yards and the areas of anaesthesia were reduced to the flexor aspect of the first toes.

Nine months later his walking distance was entirely normal and apart from occasional mild burning sensations in the toes, he was symptom free. There was no anaesthesia of the toes. His dyspeptic symptoms had gone and he had gained weight. He continued to suffer from frequent headaches but was having no medication for these. A further single oral dose of 2 mg. ergotamine tartrate was given at this time, but this caused no alteration in the foot pulses.

Investigations. Initial Hb 12.5 g/100 ml. (87%), WBC 13,000/cu.mm., normal differential, ESR 30 mm./hr. (Westergren). Provocative doses of ergotamine tartrate produced elevation of the patient's temperature, pulse rate, white cell count and ESR (Fig. 1). WR negative, no LE cells in serum. The standard biochemical tests of liver function were normal. At no time were there abnormal constituents in the urine; his blood urea remained in the region of 30 mg./100 ml. and his plasma electrolytes were normal. Creatinine clearance and plasma renin levels were normal both before and after a provocative dose of ergotamine. ECG normal; an exercise test performed after the provocative dose of ergotamine failed to demonstrate any change. A barium meal and gastric biopsy were normal.

Arteriography. A translumbar aortogram performed four days after the last dose of Migril showed the

FIG. 1—Graph illustrating the changes in right calf muscle blood flow, peripheral resistance, E.S.R., W.B.C., temperature and foot pulses following cessation of therapy and following provocative doses of ergotamine tartrate. Similar plethysmographic results were obtained for the muscle and skin flows of both legs. Peripheral Resistance measured in arbitrary units defined as mm. Hg. per ml./100 ml./min. of blood flow.

following features:

1. Localised areas of narrowing of both external iliac arteries and generalised narrowing of the right internal iliac artery.
2. Abrupt severe narrowing of both superficial femoral arteries and both profunda femoris arteries at their origins, the changes extending throughout their lengths. The popliteal arteries were slightly larger in calibre, although they also showed some narrowing (Fig. 2 A and B).
3. Further tapering of the calf vessels as far as they could be visualised.
4. Smoothness of the arterial wall at all levels.

On the next day bilateral femoral arteriograms showed reversal of these changes (Fig. 3 A and B). The width of all arteries in both legs as far as the feet was now almost normal. There was no atheroma or occlusion.

Plethysmography. Serial studies were made of blood flows in the calf and ankle of both legs by strain gauge plethysmography (Myers, 1964). Measurements were made of resting flows and of the peak flows during the reactive hyperaemia following a five minute period of arterial occlusion. The perfusion pressure at the knee (the difference between arterial systolic and venous pressures) was also determined and from the ratio of

FIG. 2.—A—Part of a lumbar aortogram four days after the last dose of ergotamine tartrate, showing narrowing of the superficial femoral and profunda arteries at their origin. B—The narrowing extends right down into the popliteal artery.

the perfusion pressure to the peak flow, the peripheral resistance in the calf during vasodilation was calculated. The changes in the calf (muscle) flows and peripheral resistance are shown in Fig. 1; essentially similar results were obtained for flows at the ankle (skin). Resting and peak flows were reduced and peripheral resistance increased, both initially and following provocative doses of ergotamine given during the acute phase of the illness. Studies performed immediately following oral ergotamine showed no change in flows within three hours. The measurements made seven weeks after the last dose of ergotamine are within normal limits. The single 2 mg. dose of ergotamine given nine months after discharge from hospital caused no change in muscle or skin flows of the lower legs.

Histology. Biopsies of skin, muscle and short saphenous vein from the lower part of the patient's right leg revealed no histological abnormality in the vein or small vessels.

Electromyography. The conduction velocity in the left lateral popliteal nerve was measured between knee and ankle; the result of 41.4 metres per second was within normal limits.

Neurological. X-rays of skull and electroencephalography revealed no abnormality, thus tending to exclude a possible intracerebral cause of the patient's headaches.

Discussion

Ergot (*Claviceps purpurea*) is a fungal parasite which grows on rye and other grains. Ergot poisoning (St. Anthony's Fire) resulting from the ingestion of contaminated rye bread, was endemic in Europe in the Middle Ages; epidemics are now rare but have occurred as recently as 1951 in France (Gabbai, Lisbonne and Pourquier, 1951). Sporadic cases of ergot poisoning now usually follow the therapeutic administration of ergotamine tartrate.

In 1883 Eulenberg first used ergot in the treatment of migraine (Friedman, Von Storch and Araki, 1959); following isolation of ergotamine by Stoll in 1918, Maier (1926) recommended its use alone for migraine. Since then ergotamine has been combined with caffeine, anti-emetics, anti-histaminics and sedatives to give a large number of preparations for the relief of migraine; the relative efficacy of these preparations and of the different routes of administration has been discussed in the literature (Greene, 1959; Crooks, Stephen and Brass, 1964).

The effect of the ergot alkaloids on the peripheral circulation is twofold, a fact recognised by Dale in 1906. There is firstly a vasoconstrictor action due to direct

FIG. 3—A, B—Right femoral arteriogram on the next day. The width of all the arteries is now virtually normal as far as the foot, with the exception of slight narrowing in the lower superficial femoral. The appearances on the left were identical.

stimulation of smooth muscle in the vessel wall, and secondly, an α -adrenergic blocking action. Which of these two actions predominates depends on the chemical configuration of the alkaloid and on the dosage employed. With the exception of ergometrine, the ergot alkaloids consist of a nucleus of lysergic acid and a polypeptide side chain. Modifications of this chain determine the vasoconstrictor activity of the alkaloid. Hydrogenation of a double bond in the lysergic acid nucleus has resulted in further variants with enhanced α -adrenergic blocking

ability and reduced vasoconstrictor activity. Ergotamine is a powerful vasoconstrictor and in relatively small doses the vasoconstrictor effect predominates, it being less intense but more prolonged than that produced by noradrenaline; in larger doses the α -adrenergic blockade becomes more apparent, but even at toxic doses this sympatholytic action is not complete.

During an attack of migraine, the extracranial arteries on the affected side of the head are abnormally dilated (Tunis and Wolff, 1952) and blood flow through them is

increased (Elkind, Friedmann and Grossman, 1964). The relief of pain obtained with ergotamine has been attributed by several authors including Elkind and colleagues (1964) to its vasoconstrictor action on these vessels.

The variety of symptoms occurring in ergot poisoning may be classified into two groups: circulatory and neurological. The circulatory changes of intense vasoconstriction in the extremities may cause intermittent claudication, paraesthesiae, burning sensations, vesicle formation and gangrene. The neurological manifestations have been described by Von Storch (1938) and include headache, vertigo, psychotic disturbances, convulsions and coma. The lumbar pain and gastric disturbances of which our patient complained have also been described.

It is difficult to assess the incidence of side-effects from ergotamine tartrate; complications are rare and possibly even less likely when the drug is used for migraine (Von Storch, 1938). The oral route of administration of ergotamine was found by Sweetnam (1961) to be the route most commonly used and yet the first case of arteriospasm in a migrainous subject following oral ergotamine was only recently reported by Byrne-Quinn (1964). He discovered twelve other reports in the literature of arteriospasm in migrainous subjects, but in all cases this had followed the administration of ergotamine by injection or suppository; none of these cases had required a major limb amputation.

This raises two questions, firstly whether migraine confers protection against the vascular effects of ergotamine and secondly whether the route of administration affects the incidence of complications. Cameron and French (1964) believe that migraine confers no such protection, whilst Young and Humphries (1961) suggest that it is the intermittent nature of the treatment in migraine which accounts for the low incidence of side effects. It is possible that migraine is a manifestation of a generalised vasomotor disorder (*Brit. med. J.*, 1964) which may afford protection against ergotamine toxicity, but this is largely conjecture. The second question concerning the effect of the route of administration on the incidence of side-effects is also undetermined. It would appear that some patients can tolerate large quantities of ergotamine given over long periods of time (Friedman, Brazil and Von Storch, 1955) whereas others develop acute toxic effects from minute doses (Sutton, 1964). This suggests that the side effects may be either cumulative (as was probable in our patient) or due to an idiosyncrasy. Accumulation could be influenced by the route of administration, together with the dosage and rates of detoxification and excretion, although these latter mechanisms are not clearly understood. If an idiosyncrasy existed then the route of administration would be less important. The lower incidence of side effects from oral compared with parenteral administration is probably due to incomplete absorption; oral ergotamine usually gives less relief in migraine than parenteral or rectal ergotamine (Greene, 1959), although the rate of absorption may be another factor in this context.

The pathology underlying the production of gangrene has been studied by various authors. In 1888, Von Recklinghausen attributed the gangrene of ergotism to intense arteriolar vasoconstriction, but Lewis and

Gelfand (1935), studying the necrosis induced in a fowl's comb by ergot, concluded that vasospasm alone did not cause gangrene and that the secondary changes of endothelial damage and stasis resulted in thrombosis and tissue necrosis. Yater and Cahill (1936) reported endothelial changes in a human case of gangrenous ergotism; they state that hyaline degeneration occurring in the vessel wall results from the vasoconstriction obstructing the vaso vasorum within the wall. Like Thompson, McClure and Landowne (1950) we found no organic changes in the small vessels of a migrainous subject with non-gangrenous arteriospasm. It seems, therefore, that structural occlusion is necessary for the production of gangrene. This is a basic pathological process which is found in other conditions of intense vasoconstriction such as frostbite (Edwards and Leeper, 1952), and Raynaud's phenomenon (Lewis, 1938; Lynn, Steiner and Van Wyk, 1955).

Arteriography has been recorded in five cases of ergot poisoning (Yater and Cahill, 1936; Young and Humphries, 1961; Allen, Barker and Hines, 1962; Johnsson, 1962), but no case with arteriographic examination has yet been reported in the British literature.

Our case illustrates the changes which have been described in ergot poisoning. The most dramatic sign is abrupt arterial narrowing, beginning in either the iliac arteries (Johnsson, 1962) or the superficial femoral arteries (Young and Humphries, 1961) and extending throughout both legs. In addition to this generalised narrowing, localised narrowing of the iliac arteries may occur, and this was the only sign in a case described by Allen and his colleagues (1962). Similar appearances have been reported in a case of chronic ergot poisoning (Johnsson, 1962) in which there was generalised arterial narrowing in both legs, becoming very severe distally where a collateral circulation was shown. In three previous cases, two reported by Johnsson (1962) and one reported by Young and Humphries (1961), the arteriogram was repeated, the interval between the two examinations being respectively nine, ten and fourteen days. In all of them the arterial changes had returned virtually to normal. Our case is the only one in which the arteriogram was repeated after a short interval (24 hours). This was performed within a few hours of the spontaneous return of the foot pulses and demonstrates the rapid and almost complete recovery of the major vessel spasm.

There was no atheroma or arterial occlusion in any of the cases so far discussed. However, in the first angiogram reported in ergot poisoning, there was an occlusion just above the ankle, with collateral circulation to the foot (Yater and Cahill, 1936). The drug had been stopped forty days earlier, and as might be expected after this interval, there was no arterial spasm. The mechanism of the formation of the occlusion in this case has been discussed. Vascular studies of the upper limbs in ergot poisoning have not been reported.

With the exception of the case of Yater and Cahill (1936), the angiograms so far reported have shown localised or generalised narrowing of the major arteries to both legs, returning to normal within a short time after stopping the drug. These signs do not occur in any other vascular disease, and are diagnostic of ergot poisoning.

In many cases with a clear history of administration of ergot and a potentially viable limb, arteriography will not be indicated. However, if this history has been overlooked, or its significance has not been appreciated, the characteristic angiographic appearances should immediately point to the correct diagnosis and it is therefore important that these radiological appearances should be more widely known.

The plethysmographic studies suggest that in addition to the changes in the major vessels there was also vasoconstriction in the distal small vessel bed and that these changes persisted for some time after disappearance of the major vessel spasm.

Tissue ischaemia and damage is the probable cause of the fever, leucocytosis and raised ESR shown in Fig. 1, although a direct action of the drug causing this cannot be excluded. Tissue damage may also have accounted for the albuminuria and raised blood ureas in the epidemic of ergotism reported by Gabbai and his colleagues (1951). However, ergotamine may have a direct effect on the kidney and Cameron and French (1960) reported a reduced creatinine clearance in a case of ergot poisoning. Rothlin and Cerletti (1949) have demonstrated in the experimental animal that ergotamine causes prolonged constriction of the renal vein, whilst Bluntschli and Staub (1949) suggest from animal experiments that the pressor action of the drug depends partly on its renal effect. We could detect no abnormality in renal function nor could we detect any consistent rise in plasma renins following provocative doses of ergotamine tartrate.

Ergotamine constricts the coronary arteries (Katz and Lindner, 1939) and its use may result in angina or myocardial infarction (Goldfischer, 1960). Despite the intense vasoconstriction in the legs there was no ECG evidence of coronary insufficiency in this patient. Although the anaesthesia of the toes was probably the result of an ischaemic neuritis we found no reduction in the conduction velocity of the left lateral popliteal nerve, measured between the knee and ankle. However, this was measured at a time when the circulation was improving and it does not take account of possible ischaemia distal to the ankle.

The treatment of ergotamine poisoning involves initially the withdrawal of the drug, and this alone may result in relief; experience with peripheral arterial emboli has shown that restoration of the circulation even after some days of severe ischaemia may result in recovery. Vasodilators have been used with varying success but it is difficult to determine how much of the improvement occurring after specific therapeutic manoeuvres is simply due to the withdrawal of ergotamine and the passage of time. Sodium nicotinate is a vasodilator strongly recommended by Thompson and his colleagues (1950).

An alternative method of increasing tissue perfusion, rather than releasing vasospasm, would be to reduce blood viscosity and the use of low molecular weight dextran (Rheomacrodex) for this purpose would seem rational. In severe cases, heparin should be administered to reduce the risk of consecutive thrombosis. Hyperbaric oxygen has been used with good effect in a case reported by Eloff, Brummelkamp and Boerema, (1963).

The value of sympathectomy or sympathetic blockade

has received attention from previous authors, with some in favour of these procedures (Young and Humphries, 1961) and some against (Cameron and French, 1960). Whilst ergotamine is exerting its maximal direct effect it is likely that this is independent of the sympathetic vasoconstrictor tone. Sympathetic denervation would probably only become effective during the stage of recovery when the direct action of the drug is abating and in this interim phase sympathetic blockade would seem a more reasonable procedure than sympathectomy. Since the pulses returned quite rapidly in our case following withdrawal of ergotamine, the temporary benefits of sympathectomy were not warranted.

The prevention of ergotamine poisoning rests largely in the hands of the prescribing physician. The drug should be used with care and the dosage kept as low as possible; the drug should not be used in the presence of contra-indications, particularly peripheral arterial disease, ischaemic heart disease or renal insufficiency. Early symptoms of toxicity such as coldness, numbness or tingling of the extremities necessitate immediate withdrawal of the drug and careful observation of the patient. Conservative treatment would be expected to be sufficient in the majority of cases.

Summary

A case is presented of severe lower limb arteriospasm due to ergotamine tartrate taken orally and sublingually for migraine.

The arterial spasm was shown by arteriography and plethysmography to affect both the large and small vessels in the lower limbs and the arteriographic appearances of abrupt narrowing of the major arteries were pathognomonic of the disease.

Systemic disturbances of fever, leucocytosis and a raised ESR were noted.

General investigation revealed no other abnormality attributable to the drug.

The incidence, manifestations and treatment of ergotamine poisoning are discussed.

We would like to thank Professor W. T. Irvine for his assistance and permission to publish this case; and Dr. David Sutton for his encouragement and for performing the arteriograms. We are grateful to Dr. L. Lange for the EEG and EMG investigations, to Dr. A. Lever for the renin estimations and to Dr. K. Porter for the histological examinations.

REFERENCES

- ALLEN, E. V., BARKER, N. W., and HINES, E. A. (1962): *Peripheral Vascular Diseases*. Third edition. Pp. 146-149. London: Saunders.
- BLUNTSCHLI, H. J., and STAUB, H. (1949): Über die Bedeutung der Nierentätigkeit für die Blutdruckwirkung eines dehydrierten Ergotderivats, Dihydroergocornin, *Experientia*, 5, 46.
- LEADING ARTICLES (1964): Vascular Response in Migraine, *Brit. med. J.*, i, 195.
- BYRNE-QUINN, E. (1964): Prolonged Arteriospasm after Overdose of Oral Ergotamine Tartrate in Migraine, *Brit. med. J.*, ii, 552.
- CAMERON, E. A., and FRENCH, E. B. (1960): St. Anthony's Fire Rekindled; Gangrene due to Therapeutic Dose of Ergotamine, *Brit. med. J.*, ii, 28.

- CAMERON, E. A., and FRENCH, E. B. (1964): Correspondence. Prolonged Arteriospasm after Ergotamine, *Brit. med. J.*, ii, 875 and 949.
- CROOKS, J., STEPHEN, S. A., and BRASS, W. (1964): Clinical Trial of Inhaled Ergotamine Tartrate in Migraine, *Brit. med. J.*, i, 221.
- DALE, H. H. (1906): On some Physiological Actions of Ergot, *J. Physiol.*, 34, 163.
- EDWARDS, E. A., and LEEPER, R. W. (1952): Frostbite. Analysis of 71 Cases, *J. Amer. med. Ass.*, 149, 1199.
- ELKIND, A. H., FRIEDMANN, A. P., and GROSSMAN, J. (1964): Cutaneous Blood Flow in Vascular Headaches of the Migraine Type, *Neurology (Minneapolis)*, 14, 24.
- ELOFF, S. J., BRUMMELKAMP, W. H., and BOEREMA, I. (1963): A Case of "Ergot Foot" Treated with Hyperbaric Oxygen Drenching, *J. Cardiovasc. Surg. (Torino)*, 4, 747.
- FRIEDMAN, A. P., BRAZIL, P., and VON STORCH, T. J. C. (1955): Ergotamine Tolerance in Patients with Migraine, *J. Amer. med. Ass.*, 157, 881.
- FRIEDMAN, A. P., VON STORCH, T. J. C., and ARAKI, S. (1959): Ergotamine Tartrate: its History, Action and Proper Use in the Treatment of Migraine, *N.Y. St. J. Med.*, 59, 2359.
- GABBAI, LISBONNE and POURQUIER. (1951): Ergot Poisoning at Pont St. Esprit, *Brit. med. J.*, ii, 650.
- GOLDFISCHER, J. D. (1960): Acute Myocardial Infarction Secondary to Ergot Therapy, *New Engl. J. Med.*, 262, 860.
- GREENE, R. (1959): Drug Treatment of Disease. Migraine, *Brit. med. J.*, i, 574.
- JOHNSSON, K. A. (1962): Angiography in Two Cases of Ergotism, *Acta Radiologica*, 57, 280.
- KATZ, L. N., and LINDNER, E. (1939): Reaction of Coronary Vessels to Drugs and Other Substances, *J. Amer. med. Ass.*, 113, 2116.
- LEWIS, T. (1938): Pathological Changes in Arteries Supplying Fingers in Warm Handed People and in Cases of so-called Raynaud's Disease, *Clin. Sci.*, 3, 287.
- LEWIS, T., and GELFAND, B. (1935): The Manner in which Necrosis Arises in the Fowl's Comb under Ergot Poisoning, *Clin. Sci.*, 2, 43.
- LYNN, R. B., STEINER, R. E., and VAN WYK, F. A. K. (1955): Arteriographic Appearances of the Digital Arteries of the Hands in Raynauds Disease, *Lancet*, i, 471.
- MAIER, H. W. (1926): L'ergotamine, Inhibiteur due Sympathique Etudié en Clinique, Comme Moyen d'Exploration et Comme Agent Thérapeutique, *Rev. Neurol.*, 33, 1104.
- MYERS, K. (1964): The Investigation of Peripheral Arterial Disease by Strain Gauge Plethysmography, *Angiology*, 15, 293.
- ROTHLIN, E., and CERLETTI, A. (1949): Untersuchungen über die Kreislaufwirkung der Ergotamin, *Helv. physiol. Acta*, 7, 333.
- SUTTON, R. A. L. (1964): Correspondence. Arteriospasm after Ergotamine Therapy, *Brit. med. J.*, ii, 756.
- SWEETMAN, M. T. (1961): An Enquiry into the Treatment of Migraine, *J. Coll. gen. Practit.*, 4, 538.
- THOMPSON, W. S., MCCLURE, W. W., and LANDOWNE, M. (1950): Prolonged Vasoconstriction due to Ergotamine Tartrate, *Arch. intern. Med.*, 85, 691.
- TUNIS, M. M., and WOLFF, H. G. (1952): Analysis of Cranial Artery Pulse Waves in Patients with Vascular Headache of the Migraine Type, *Amer. J. med. Sci.* 224, 565.
- VON RECKLINGHAUSEN (1888), Handbuch der Allgemeinen Pathologie. Stuttgart.
- VON STORCH, T. J. C. (1938): Complications Following the Use of Ergotamine Tartrate, *J. Amer. med. Ass.*, 111, 293.
- YATER, W. M., and CAHILL, J. A. (1936): Bilateral Gangrene of Feet Due to Ergotamine Tartrate used for Pruritis of Jaundice, *J. Amer. med. Ass.*, 106, 1625.
- YOUNG, J. R., and HUMPHRIES, A. W. (1961): Severe Arteriospasm after Use of Ergotamine Tartrate Suppositories, *J. Amer. med. Ass.*, 175, 1141.

DISSEMINATED HISTOPLASMOSIS AND ITS TREATMENT

BETTY M. PARTRIDGE, M.A., Ph.D.* A. R. TANSER, M.B., M.R.C.P.

King's College Hospital, London, S.E.5.

DISSEMINATED histoplasmosis is the most serious form of the disease produced by the fungus *Histoplasma capsulatum*. Only five cases of this type have been reported in Britain (Derry, Card, Wilson, and Duncan, 1942; Lockey, Atkinson, Grieve, and Bridson, 1953; Poles and Lavertine, 1954; Earle, Highman, and Lockey, 1960; Miller, Ramsden and Geake, 1961).

Histoplasmosis, first described by Darling in 1906, is common in N. America and Asia. Patients seen with histoplasmosis in this country have usually contracted the disease abroad; endemic infection is rare (Symmers, 1956). This paper describes a case of disseminated histoplasmosis, probably contracted in Malaya, and its successful treatment with amphotericin B.

Case Report

Mrs. J. M., an Englishwoman, aged 42, lived in Malaya for nine years, with brief visits to India and Ceylon. During her sojourn, she experienced several bouts of fever of unknown origin, the last attack in 1959 necessitating hospital treatment. Later in 1959, a three month trip in the U.S.A., from Washington through Alabama and Tennessee to Los Angeles and San Francisco, was followed by visits to Japan, Hawaii and Hong Kong. Afterwards she returned to England.

* Bacteriology Department (under tenure of personal grant from M.R.C.)

Present address: Charing Cross Hospital Medical School.