Treatment.—Despite the wealth of descriptive case reports, very little has been said about the treatment of fetishism. A search of the literature has revealed only three cases in which successful treatment was claimed.

1. A case seen by Krafft-Ebing is referred to by Hirschfeld (1939) as "one of those rare cases in the literature of sexual pathology in which a therapeutic success has been achieved." The patient was a limp fetishist who, after he married an understanding woman, was "educated" by his wife and eventually cured of his fetishism.

2. Romm (1949), in a notable case report, states that after 662 hours of analysis over six years, the patient (a hair fetishist) achieved a genital relationship with his wife. In the social and business spheres he became much more effective. On rare occasions, when under environmental stress, he had fetishistic fantasies but with no impulses to action. He retained a more than usual interest in his wife's hairdress.

3. Mitchell, Falconer, and Hill (1954) reported a case of temporal lobe epilepsy in which the viewing of a fetish object precipitated seizures. Relief of both the epilepsy and the fetishism followed temporal lobectomy.

Discussion

To use aversion therapy in treating this patient seemed a logical approach if one believed that the results obtained in alcoholism are not dependent upon the specific biochemical changes produced by any drug but upon the establishment of a conditioned response. The fetishist's predisposition propounded by Binet as a general nervous hyperaesthesia may well be expressed as an unusual capacity for forming conditioned responses, and this capacity might prove as great an asset in treatment as it was a liability when the fetish was formed. To use nausea and vomiting as a means of producing the aversion was clearly less appropriate than in alcoholism, but familiarity with the procedure, the ease of administration, and reluctance to use other available stimuli favoured its use. Also the modification of attitudes and psychological conversions are more easily obtained in states of exhaustion and hunger, and from that point of view the technique was suitable.

It was thought that should aversion be successfully established there might be some risk that impotence would ensue. According to Freud's (1928) view, overt homosexuality might emerge if the protective fetish objects were removed; while Stekel's (1930) experience suggested that this would happen anyway. East and Hubert (1939) stress the danger of changing a sexual fetish into strong homosexual or sadistic drives by treatment. So far none of these eventualities has arisen.

Romm's case is interesting because apparently the impulses to aggressive action disappeared or were controlled, although unusual interest in what had been the fetish object still remained, and was even occasionally used in fantasies.

Much of what our patient says—for example, that he makes mistakes about perambulators—also indicates that the habits of observation persist to some extent. He insists, however, that observation is more casual, and that sexual stimulation never occurs as a result.

Summary

A report is given of a case of fetishism believed to be unique in that the patient responded favourably to aversion therapy. A brief review of the literature is given and discussed in relation to the treatment of this case. It is suggested that the predisposition to fetishism, first discussed by Binet, may lie in an unusual capacity to form conditioned responses, and that this capacity may be used as an asset in treatment.

I am indebted to Dr. Desmond Curran for the opportunity to treat this patient, and for permission to publish this report. I also thank him and Sir Paul Mallinson for much helpful criticism and advice in the preparation of this paper. It is a pleasure to acknowledge the help and co-operation of the nursing staff at Atkinson Morley's Hospital.

REFERENCES

- Binet, A. (1888). *Etudes de Psychologie Expérimentale*. Paris.
Curran, D. (1954). *Practitioner*, 172, 440.
Descartes, R. (1649). *Les Passions de l'Âme* (CXXXV).
East, W. Norwood (1949). *Society and the Criminal*. H.M.S.O., London.
— and Hubert, W. H. de B. (1939). *The Psychological Treatment of Crime*. H.M.S.O., London.
Ellis, H. (1906). *Studies in the Psychology of Sex*, vol. 5. Philadelphia.
Fenichel, O. (1945). *The Psychoanalytical Theory of Neurosis*. New York.
Freud, S. (1928). *Int. J. Psycho-anal.*, 9, 161.
Hirschfeld, M. (1939). *Sexual Anomalies and Perversions*. London.
Karpman, B. (1934). *Arch. Neurol. Psychiat.* (Chicago), 32, 577.
Kinsey, A. C., Pomeroy, W. B., Martin, C. E., and Gebhard, P. H. (1953). *Sexual Behaviour in the Female*. Philadelphia and London.
Krafft-Ebing R. von (1939). *Psychopathia Sexualis: A Medico-Forensic Study*. London.
Mitchell, W., Falconer, M. A., and Hill, D. (1954). *Lancet*, 2, 626.
Romm, M. E. (1949). *Psychoanal. Quart.*, 18, 137.
Stekel, W. (1930). *Sexual Aberrations: The Phenomenon of Fetishism in Relation to Sex*, vols. 1 and 2. London.
Thoinot, L. H., and Weyssie, A. W. (1920). *Medico-Legal Aspects of Moral Offences*. Philadelphia.

ACTION OF DIBENYLIN ON THE PERIPHERAL CIRCULATION

BY

R. S. DUFF, M.D., F.R.F.P.S., M.R.C.P.

From the Cardiological Department, St. Bartholomew's Hospital, London

"Dibenyline" (phenoxybenzamine hydrochloride) is chemically related to though much less toxic than "dibenamine." It has been thought to cause increased blood flow in many tissues by an action mainly involving the vasomotor nerves. Studies with dibenyline in patients with peripheral vascular disease have yielded conflicting results. Moser *et al.* (1953), Haimovici (1951), Friend and Edwards (1954), and Wertheimer *et al.* (1954) found it valuable when given intravenously or orally in the treatment of vasospastic disorders, causalgia, and acrocyanosis. Wertheimer *et al.* (1954) claimed some benefit in arteriosclerosis obliterans, but most workers consider the drug to be less efficacious in organic vascular disorders.

Animal investigations have suggested that the vascular response to dibenyline is largely dependent upon an adrenergic blocking action on the sympathetic nervous system (Nickerson *et al.*, 1953; Green *et al.*, 1954; Harvey and Nickerson, 1954).

The present investigation was designed to assess the effect of the drug on diseased blood vessels and to study the role of the sympathetic nerves in the response to dibenyline in man.

Subjects and Methods

The blood flow responses of 22 sympathectomized limbs to dibenyline were studied. Most patients were given dibenyline while still in hospital in the immediate post-operative period following surgical sympathectomy. A few were tested with the drug as out-patients after sympathectomy.

The subjects belonged to one of two fairly distinct categories: (1) patients with hyperhidrosis or uncomplicated Raynaud's phenomenon who had no evidence of organic vascular disease and were therefore considered to have comparatively healthy blood vessels (eight limbs); and (2) patients with arteriosclerosis, scleroderma, or Raynaud's disease with ischaemic lesions, in whom there was undoubtedly organic vascular change (14 limbs). The effects of intravenous and of intra-arterial dibenyline were separately investigated.

The blood flow in the limbs was measured in each case by venous occlusion plethysmography, under standard conditions (Barcroft and Swan, 1953). Each limb under observation was enclosed in a neatly fitting thin rubber sheath and inserted into a plethysmograph of appropriate design. Throughout every test the temperature of the water surrounding the segment of limb in the plethysmograph was kept at $34 \pm 1^\circ \text{C}$; the room temperature was maintained between 23° and 25°C . Regular measurements of blood flow were made at intervals of half to one minute; the systemic blood pressure was recorded with a sphygmomanometer every five to ten minutes.

Control observations of blood flow were made for at least ten minutes. An intravenous or intra-arterial infusion of saline was then set up, using a power-driven infusion apparatus delivering saline at a constant rate of 3 ml. a minute (Duff, 1952). Saline alone was infused for ten minutes; the desired amount of dibenylin was then added, after which the plain saline infusion was resumed. Blood flow was measured regularly throughout the entire period.

In the studies in which dibenylin was given *intravenously* the total dose was determined by the size and condition of the patients, and was between 25 and 60 mg. The drug was infused at a rate of 0.5 to 1 mg. a minute.

In the study of *intra-arterial* dibenylin unilateral infusions were given into the brachial artery just above its bifurcation. The total dose was under 0.5 mg., given at a rate of 50 to 200 μg . a minute.

Evidence that the vasomotor nerves had been effectively interrupted in the investigated limbs was provided both clinically and by the use of the plethysmograph. Increased warmth of the skin and absence of sweating were noted; in addition Horner's syndrome was observed in those having stellate ganglionectomy. In most subjects an increase in blood flow was recorded soon after operation; however, a failure to induce vasodilatation after indirect warming of the body was regarded as the most reliable indication of successful sympathectomy (Landis and Gibbon, 1933).

Effects of Intravenous Dibenylin on Sympathectomized Vessels

Healthy Vessels

Results of a typical experiment are portrayed in Fig. 1. Bilateral cervicodorsal ganglionectomy had been performed seven days previously in a young woman with uncomplicated Raynaud's phenomenon. Soon after the start of the dibenylin infusion the blood flow in the hand increased from about 8 to over 25 ml. per 100 ml. a minute. The flow was still elevated three hours later. However, 24 hours later the

FIG. 1.—Blood flow in hand and forearm of a woman aged 27, with uncomplicated Raynaud's phenomenon, on seventh day after sympathectomy, during infusion of saline (shallow block) and dibenylin (deep block). With dibenylin the circulation increased greatly in hand, slightly in forearm. One month later blood flow in both tissues was below control level.

mean hand blood flow had returned to about the resting (pre-dibenylin) level. The increased blood flow was therefore of comparatively brief duration, and at an examination one month later the blood flow was still low.

Increased blood flow through comparatively healthy vessels after intravenous dibenylin is also shown in Fig. 2. This subject, a woman aged 37, had had bilateral cervico-

FIG. 2.—Circulation in sympathectomized hands of a woman aged 37 during continuous intravenous saline infusion. Dibenylin given between 40th and 70th minute (dotted line) was accompanied by some increase in flow in both hands, especially the right.

dorsal ganglionectomy ten days previously. A mean increase in hand blood flow of between 50 and 100% was recorded during the infusion of 45 mg. of dibenylin.

Diseased Vessels

Dibenylin caused little or no increase in blood flow in some of the subjects in this group. Findings in a man aged 53 with intermittent claudication due to arteriosclerosis of the lower limbs are illustrated in Fig. 3. Five days previously bilateral lumbar sympathectomy had been performed.

FIG. 3.—In this patient, a man aged 53 who had undergone sympathectomy for intermittent claudication, 60 mg. of dibenylin failed to influence the blood flow in the feet.

A slight increase in the blood flow in the feet had resulted from the operation. No further increase in flow occurred with intravenous dibenylin even when 60 mg. had been given. Seven weeks later the blood flow in both feet was at the pre-operative level.

In other subjects with organic vascular disease dibenylin did increase the blood flow. The circulatory response in the hands to an infusion of 25 mg. of dibenylin in a woman with scleroderma is shown in Fig. 4. An increase in flow

FIG. 4.—Intravenous dibenylin caused some increase in flow in both hands of a woman aged 65 with diseased blood vessels,

of approximately 100% occurred in both hands. The flow was no longer raised two months after the infusion. This patient had obtained little or no symptomatic relief from bilateral cervicodorsal sympathectomy nine years previously, or from vasodilator drugs such as tolazoline hydrochloride. She claimed considerable relief from a subsequent course of oral dibenylin.

Effects of Intra-arterial Dibenylin

In this series a regular infusion of saline into the brachial artery of the right arm was maintained continuously. At half-minute intervals the blood flow was measured simultaneously in both hands. After a control period of five to ten minutes dibenylin was added to the infusion in an amount sufficient to produce a concentration between 50 and 200 μ g. a minute. This was given for four minutes; then, after a further control period on saline alone, a second infusion of dibenylin was given.

The total amounts of dibenylin were too small to have any measurable effect on systemic blood pressure or on blood flow in the non-infused left hand.

Healthy Vessels

Dibenylin caused a marked increase in blood flow in the infused right hand without affecting the level of flow in the left hand.

Fig. 5 illustrates the response in a man of 48 with coronary disease but otherwise healthy blood vessels. Six days before the test bilateral cervicodorsal ganglionectomy had been performed, and Horner's syndrome and anhidrosis of the denervated areas had resulted. The blood flow in the infused right hand averaged 7 ml. per 100 ml. a minute during the initial saline control period. Soon after adding dibenylin at a concentration of 100 μ g. a minute the blood

flow in the right hand rose to between 12 and 13 ml. On resuming the plain saline infusion the flow in that hand fell slightly, but when dibenylin was given again, at 200 μ g. a minute, a further increase in flow occurred, to between 14 and 16 ml.

Fig. 5 illustrates the important control provided by the non-infused left hand which failed to exhibit any increased flow. This confirmed that the dibenylin did not escape from the right hand in an amount sufficient to cause systemic effects on the peripheral circulation. No change in heart rate or arterial blood pressure was recorded during the intra-arterial infusions of these small amounts of dibenylin.

FIG. 5.—Two infusions of dibenylin into the right brachial artery caused increase in blood flow in the right hand of a man aged 48, with angina, on the sixth day after bilateral cervicodorsal sympathectomy.

Diseased Vessels

Similar responses were recorded in patients sympathectomized for peripheral vascular disease of the upper extremity. The results of one such test are illustrated in Fig. 6. The blood flow was measured in both hands of a woman of 39 who had had bilateral cervicodorsal ganglionectomy eight days previously. A continuous infusion into the right brachial artery was maintained throughout the period of observation. During the initial saline control period the blood flow in the right hand averaged about 12 ml. per 100 ml. a minute. Soon after adding dibenylin to the intrabrachial infusion (at a rate of 100 μ g. a minute) the flow in the right hand rose to over 20 ml. This marked

FIG. 6.—Intra-arterial dibenylin caused vasodilatation confined to the infused hand of a woman aged 39, with Raynaud's phenomenon and calcinosis, sympathectomized eight days previously.

increase in flow with dibenylin was not invariably found. A young girl of 15 was studied five days after cervicodorsal ganglionectomy for hyperhidrosis. Only a slight increase in flow accompanied infusions of dibenylin in concentrations of 50 and 200 μ g. a minute. In none of the tested subjects, however, was dibenylin associated with a reduction of flow in the infused hand, and the common response, irrespective of the condition of the blood vessels, was a distinct increase in blood flow.

Discussion

This study has shown that in man dibenylin is capable of increasing the blood flow through vessels surgically deprived of their sympathetic innervation. The increase in flow after intravenous dibenylin was generally greater in subjects with little or no organic arteriolar narrowing than in those with structural ischaemic change. The volume of blood flowing through any part of the arterial tree is determined by the "perfusing" pressure and by the vascular resistance. In these experiments there was no increase in pressure; on the contrary, the blood pressure generally fell a little with the intravenous infusions of dibenylin. The increased flow was therefore due to a lowering of resistance—that is, to an increase in mean vascular calibre. Since the blood vessels had been denervated the increased flow was not due to any effect of dibenylin on the sympathetic nerves. The vasodilatation could therefore be attributed to an action of the drug at the periphery or to the systemic release of some vasodilator substance by the intravenous dibenylin.

The mechanism was further elucidated by the studies using intra-arterial dibenylin. Dilatation during infusion of the drug into the brachial artery was confined to the corresponding hand. This demonstrated that the vasodilatation with dibenylin can result from a purely peripheral action without involving any systemic or central effect. This peripheral action presumably involves the receptor elements or the contractile muscle of the arterioles.

In subjects with intact vasomotor nerves this action is no doubt reinforced by the effects of the drug (when given orally or intravenously) on the sympathetic nervous system. It has been demonstrated that dibenylin is capable of dilating blood vessels by peripheral action beyond the sympathetic terminals. This is of particular importance in patients in whom the vasomotor nerves have been ablated by surgery or impaired by metabolic or nutritional disorders. Dibenylin is specially indicated in acute ischaemia of an extremity, for it may be infused directly into the artery of any limb to which the vascular disturbance is confined. It is effective in doses that do not influence the blood pressure or systemic circulation.

If two or more limbs are involved the drug may be given intravenously in larger amounts (25–60 mg.). By this route its systemic actions, especially its tendency to lower the blood pressure, may be a disadvantage.

Undesirable effects tend to occur with intravenous doses of over 40 mg. of dibenylin. The most serious of these—tachycardia and hypotension—are related to the widespread vasodilatation produced. The drug is therefore best withheld from people known to have heart disease. After intravenous administration all patients should be kept in bed for 24 to 48 hours, and the heart rate and blood pressure carefully watched. Some drowsiness and lethargy is to be expected during this period, but requires no treatment. Nasal stuffiness due to congestion of the mucosae is common, but rapidly passes off. If dibenylin is given continuously by mouth, especially in daily doses greater than 20 mg., nasal congestion, lethargy, and giddiness may occur, but considerable relief is usually afforded by the use of an amphetamine inhaler and small doses of dexamphetamine sulphate tablets, *B.P.C.*

Summary

It has been shown that dibenylin is capable of increasing the blood flow in the limbs by a peripheral action independent of any effects it may have on the sympathetic nervous system.

The vasodilatation from a single injection is of rapid onset and persists for several hours.

The drug may be of particular value in treating acute ischaemia of a limb, for it is effective when infused intra-arterially in doses (under 0.5 mg. into the brachial

artery) that do not appreciably affect the general circulation.

Dibenylin is effective even in patients in whom the integrity of the vasomotor nerves has been lost.

However, it must always be remembered that the extent to which any blood vessel may dilate with dibenylin or with any other agent is determined ultimately by the degree to which disease has induced structural change in the vessel wall.

The patients were investigated by courtesy of Professor Sir James Paterson Ross, Professor J. B. Kinmonth, and Mr. G. W. Taylor, to whom I am much indebted. For valuable encouragement and advice I am grateful to Dr. Geoffrey Bourne and Dr. Graham Hayward, of St. Bartholomew's Hospital, and to Professor Henry Barcroft and Dr. Jean Ginsburg, of St. Thomas's Hospital Medical School. I would like also to thank Dr. Kenneth Carter and the secretarial staff of Smith, Kline and French International Co. for supplies of dibenylin and for secretarial help.

REFERENCES

- Barcroft, H., and Swan, H. J. C. (1953). *Sympathetic Control of Human Blood Vessels*. Arnold, London.
 Duff, R. S. (1952). *J. Physiol. (Lond.)*, **117**, 415.
 Friend, D. G., and Edwards, E. A. (1954). *A.M.A. Arch. intern. Med.*, **93**, 928.
 Green, H. D., Denison, A. B., Williams, W. O., Garvey, A. H., and Tabor, C. G. (1954). *J. Pharmacol.*, **112**, 462.
 Haimovici, H. (1951). *Angiology*, **2**, 531.
 Harvey, S. C., and Nickerson, M. (1954). *J. Pharmacol.*, **112**, 274.
 Landis, E. M., and Gibson, J. H., jun. (1933). *Arch. intern. Med.*, **52**, 785.
 Moser, M., Prandoni, A. G., Orbison, J. A., and Mattingly, T. W. (1953). *Ann. intern. Med.*, **38**, 1245.
 Nickerson, M., Henry, J. W., and Nomaguchi, G. M. (1953). *J. Pharmacol.*, **107**, 300.
 Wertheimer, L., Redisch, W., and Steele, J. M. (1954). *Circulation*, **10**, 366.

CARDIOVASCULAR COLLAPSE DURING APOMORPHINE TREATMENT

BY

DENIS PARR, M.D., D.P.M.

Department of Psychiatry, St. George's Hospital, London

Apomorphine treatment for alcoholism is being used on an increasingly large scale, and published reports suggest that it is effective and safe. In principle, the method, which was introduced by Dent in 1934, consists in giving drinks of alcohol together with subcutaneous or intramuscular injections of apomorphine repeatedly over a few days. There has recently been a trend, expounded chiefly by Feldmann (1952), of Geneva, towards long and intensive courses of treatment, such as apomorphine 1/10 gr. (6.5 mg.) by injection and alcohol by mouth, two-hourly day and night for six to ten days, during which time other foods and fluids are absolutely withheld.

In view of the safety claimed for this treatment, it is thought worth publishing the following observations on a patient who showed an anomalous and dangerous reaction to apomorphine. In spite of his experiences under therapy, he generously volunteered to have further doses of the drug experimentally, and thereby made it possible for the nature of this unusual reaction to be more accurately defined.

Case History

The patient, a man of 32, was of markedly asthenic physique and had a thoracic kyphoscoliosis. He had a history of repeated attacks of intestinal colic, which had not been cured by a reconstruction operation carried out on the hypothesis that an aberrant mesenteric vessel might be responsible. He came under psychiatric treatment because of a confusional state provoked by drugs and alcohol. The most notable feature in his drug-taking history was the injection of pethidine in doses up to 2,500 mg. daily, intermittently