MIGRAINE: A 1950 SYMPOSIUM

By N. N. IOVETZ-TERESHCHENKO, F.R.C.S.

Definition

The disease, also called *megrim* consists of recurring attacks of severe headache, usually unilateral (hence the synonym *hemicrania*), sometimes preceded by certain abnormal sensations, most commonly disorders of vision, and often associated with nausea and vomiting (hence the synonyms *sick headache* and *bilious headache*).

Incidence

It is estimated to occur in 8 to 12 per cent. of all patients seen in general practice (Grimes, 1931). In the United States 2 to 4 per cent. of the total population suffer from migraine (Moench, 1947). Two factors are to be considered:

1. *Sex*. It is more frequent in women than in men in a ratio of four to one according to von Storch (1947), the attacks being sometimes closely related to menstruation. Pregnancy usually gives complete relief (Alvarez, 1947).

2. *Age*. It commonly begins in adolescence at about the age of puberty, but often a history of previous 'bilious attacks' in childhood may be obtained (the so-called 'cyclical vomiting' of children appears to be a condition closely allied to migraine). More rarely the complaint develops in later years and still more rarely in early childhood or infancy (Sinkler, 1887, refers to a case in a child aged two years). Having once appeared, the paroxysmal headaches usually persist throughout life, with a definite tendency to diminish in frequency and severity, and even to disappear, after the menopause in women and the age of about 50 in men.

Aetiology

Apart from certain clinical resemblances, there is an association between migraine and epilepsy; they sometimes both occur in the same patient and, in certain instances, epilepsy has disappeared (Wilson, 1925) giving place to migrainous attacks and vice versa.

HEREDITY

Heredity plays an important role in some 90 per cent of cases (Möbius, 1894), a family history of the disease being obtainable from a large proportion of patients. Personality is an important

factor (Wolff, 1940), the individual affected being usually an ambitious perfectionist in a continuous state of tension (Whitehorn, 1944). The prime and most common cause appears to be a constitutional defect transmitted through the germ plasm in accordance with Mendel's laws of inheritance (Buchanan, 1920).

PRECIPITATING FACTORS

As in the case of epilepsy, the great majority of attacks occur without apparent cause. Many have been described as predisposing to and as occasional immediate causes of the attacks.

1. *Mental strain* is the commonest. This apparently explains the relative frequency of migraine among intellectual (as opposed to manual) workers and 'highly strung' persons of excitable disposition.

2. *Eye strain* is an important factor, especially when resulting from uncorrected errors of refraction, or of muscle balance, or from reading or writing for prolonged periods in a bad light or incorrect posture.

3. *Vasomotor disturbances*, characterized either by spasm of the arteries, causing the temporary paralysis which may be associated with a monoplegic or hemiplegic attack, or by paralysis of the vasomotor centre, with consequent capillary engorgement.

4. *Toxaemia* from disorders of digestion or intestinal function (constipation or dietetic indiscretions may initiate paroxysms) or from self-manufactured poisons (dental sepsis, sinusitis or other septic foci such as chronic cervicitis or appendicitis).

5. *Allergy* is probably responsible for a certain number of cases (Unger, 1940), many of which are sensitive to some particular kind of food (Wolff and Unger, 1944) and some even may be simultaneously suffering from hay fever or asthma.

6. *Hepatic dysfunction* (Diamond, 1927; McClure and Huntsinger, 1928; Critchley and Ferguson, 1933) perhaps with sub-acute hepatitis and/or gall-bladder disease (Chiray and Triboulet, 1925; Vallery-Radot and Blamoutier, 1927; Friedlander and Petow, 1927; Lyon, 1929; Haug and Wohrmann, 1930; Hunt, 1933) is suggested in many patients (see also Morlock and Alvarez, 1940).

7. *A neurotic manifestation* may be the explanation, as in the case where trauma, often not very severe, is blamed several years after the event for persistent paroxysmal headaches which began after the accident.

8. *Reflexes* from pathological conditions in the nose or genital organs have been considered by some as a cause (this may be brought into line with the paragraphs on *toxaemia* and *hepatic dysfunction* above).

9. Finally, the presence of a gross *anatomical defect* causing stenosis of the interventricular foramen of Monro and associated with chronic hyperaemia of the choroid plexus, is the view held by Spitzer (1901) and nobody else.

Pathology

No macroscopic anatomical changes have been found to account for the disease, except in the exceedingly rare cases having a congenital stenosis of the foramen of Monro.

The association of visual disturbances, slowing of the pulse rate, headache, vomiting and (sometimes) cramps or spasms in the cranial and cervical muscles of the affected side, with temporary aphasia and/or hemiplegia, suggests three possible explanations:

1. A mechanical obstruction to the outflow of the cerebrospinal fluid from the ventricles, producing for the time being an internal hydrocephalus.

2. A transient paralysis of the vasomotor centre with consequent capillary engorgement and oedema of the brain.

3. A spasm of the arteries supplying various parts of the central nervous system, causing a partial and temporary ischaemia of the part in question.

The aura is apparently due to vasoconstriction of the branches of the internal carotid artery, with consequent anoxia, especially of the occipital cortex (Schumacher and Wolff, 1941). The headache seems to be chiefly due to distension and increased amplitude of pulsation of the intracranial branches of the external carotid artery, the wall of the affected arteries becoming rigid and often ceasing to respond to vasoconstrictor stimuli (Torda and Wolff, 1945). In addition spasmodic or sustained contraction of the cervical or scalp muscles on the affected side results in further pain and in cranial tenderness (Simons, Day, Goodell and Wolff, 1943). The pain reaches consciousness mainly through the fifth cranial nerve (Rowbotham, 1942) but also, though to a lesser degree, through the ninth and tenth cranial nerves and the upper three cervical roots (Ray and Wolff, 1940).

Abnormal suprarenal function has been supposed to play a part (Hellwig, 1924) and 'periodic

dilatation' of the stomach has been observed during severe attacks (Mangelsdorf, 1903). Poussepp (1925) considers that swelling of the pituitary and its consequent compression by an abnormally small sella turcica play an important part in initiating an attack of migraine.

It may be mentioned here that the blood glucose is often low at the onset, that there is sometimes an eosinophilia of 5 to 15 per cent. (Gänsslen, 1921) and that in severe attacks there is complete cessation of gastric peristalsis as seen on radiological examination.

Symptoms

A typical attack consists of (1) an aura; (2) the headache; and (3) visceral disturbances (nausea, vomiting, occasionally diarrhoea). Any of these may occur without the others, the headache being practically always present and most frequently associated with nausea.

The attack may last from a few hours to several days, one day being the usual duration. Disappearance of the headache may quickly follow vomiting, or it may subside more gradually, the patient going to bed at night with the headache to awake cured with only, perhaps, some sense of weakness or fatigue. The attacks may recur at intervals of a few days to two or three months, an interval of three to four weeks being most common. Their paroxysmal character may be a striking feature of the attacks, which may occur on the same day every week or every month.

Migraine equivalents. A few patients have curious abdominal attacks regarded as an equivalent of migraine (Brams, 1922; Riley, 1932; van der Scheer, 1938) and possibly allergic in origin. Colic in children may also be really migraine (Soltz, Brickner, Riley and Salmon, 1935; Curschman, 1939). Ménière's syndrome is believed (Atkinson, 1943) to be an occasional substitute for migraine. 'Precordial migraine,' characterized by dull, heavy, left thoracic pain with occasional radiation into axilla or arm, has been described (Fitz-Hugh, 1940). A 'psychic' equivalent (moodiness, confusion, anxiety, agitation and general restlessness) has also been described (von Storch, 1947) and can be differentiated from the psychomotor equivalent of epilepsy only by a normal encephalogram taken during sleep.

The aura. An aura is not always present; if present it lasts from a few minutes to half an hour, typically taking the form of a visual disturbance.

Most frequently there are only vague flashes of light followed by darkness in the half-field involved, or a simple onset of hemianopic dimness of vision (the part of the visual field affected varying

from one attack to another). Commonly only a general dimness of vision is present. Sometimes apparitions may be seen in the shape of hallucinatory visions of animals such as mice, dogs, etc. Rarely a complete 'fortification spectrum' (known as *teichopsia*) is present: the patient notices a blind spot in the centre of his field of vision (usually in both eyes, rarely in one only), which soon becomes replaced by a bright spot of light; the area of blindness enlarges in a few minutes and if the patient turns to a dark part of the room he will see an irregularly circular patch of gorgeously sparkling colours; from minute to minute the circle grows larger and larger until it opens out in the form of a horseshoe, the outer margin of which consists of a multicoloured zig-zag line enclosing a central blind area apparently full of movement as of a boiling fluid; the opening as a rule is to one side and away from the centre and the area of recovered vision is within the restless stirring blind field. In 20 to 30 minutes from the beginning of the manifestation, the brilliant horseshoe reaches the periphery of the visual field, every object now becoming visible, but apparently oscillating or quivering as in a dream.

The visual aura may be followed or replaced by sensory or motor premonitory signs with the same distribution as that of a hemiplegia. These usually begin with tingling in the tongue and lips then in the face and hand, the part first attacked recovering as the next one is invaded. More rarely cramps and spasms of the muscles of the affected side and even occasionally paresis or paralysis (monoplegia or hemiplegia) occur. When the right side is affected there is usually a temporary aphasia (compare with Jacksonian epilepsy and Todd's paralysis).

In some cases there may be hunger, dizziness or excitement; more commonly there is mental confusion and great depression, with fear of impending evil. Rarely there is an unusual sense of well being.

Headache. This is almost invariably present, coming on as a rule immediately after the aura. The side first affected is generally that which is opposite to the visual spectrum. The pain commonly starts in a localized spot and spreads in differed directions (i.e. is expansile in character) or becomes general. The pain is often described as penetrating, sharp and boring in character, and varies in intensity from so slight as not to interfere with mental work, to so intensely severe as entirely to unfit the sufferer from any action whatsoever. The pain is usually aggravated by movement, light or sound, and the patients are most comfortable in the recumbent posture. Occasionally the severity is such that the patient passes into a stupor or becomes delirious.

Visceral disturbances. Nausea and vomiting are common, and a certain amount of relief follows, especially if the attack comes on when the stomach is full.

Other manifestations. In a small proportion of patients in addition to or instead of the usual nausea and vomiting there may be present tremors, vertigo, dryness of the mouth, excessive sweating, coldness of the extremities and abdominal distension.

Status migrainicus. Very rarely the periodic attacks may fuse into a continuous episode, prolonged for days, with excessive gastro-intestinal symptoms.

Physical Signs

In the interval between the attacks no abnormal physical signs are present except in certain very rare cases in which there are signs of sclerosis of the retinal arteries on the affected side.

During an attack the pulse is usually small, feeble and slow, the hands and feet are cold, the face is pale and drawn (though in some cases, towards the end of the attack, the face flushes and sweating occurs), with sometimes marked differences between the two sides. The temporal artery on the affected side is often firm and hard and the retinal arteries may be seen to be in spasm. In some instances there is a spasmodic action, alternate dilatation and contraction, of the pupil on the affected side, a condition known as *hippus*.

In the comparatively rare type called *ophthalmoplegic migraine* the headache is associated with a temporary paralysis of one of the oculo-motor nerves, a paralysis which may in the course of time become permanent (Riley, 1932).

Diagnosis

This is usually easy: the age of onset, the periodicity of the attacks with intervals of complete freedom, the association with nausea and vomiting and, in many cases, the family history are as a rule sufficient.

Some patients may be troubled by the nausea or vomiting more than by the headache, and accordingly seek relief for these symptoms only (Alvarez, 1947), but a careful clinical history will clinch the diagnosis.

DIFFERENTIAL DIAGNOSIS

Recurring headaches of the migraine type may also occur in the following conditions:—

Cerebral tumour, which is sooner or later always associated with papilloedema and other signs of local damage to the brain.

Chronic nephritis. The aura is absent and signs of renal involvement are to be found.

Infection of nasal sinuses, which must be excluded

clinically and radiologically in all cases with attacks of severe headache.

Toxic causes, such as uraemia, should and usually can be distinguished with comparative ease.

Meningo-vascular syphilis, when the Wassermann reaction and other appropriate tests are usually positive both in the blood and in the cerebrospinal fluid.

Cerebral arterio-sclerosis, always accompanied by other signs of arterial disease.

Hypertension presents as a rule no special difficulty in diagnosis.

Temporal arteritis is often accompanied or preceded by general malaise, low fever and leucocytosis, while locally the skin over the painful area is reddened and the superficial temporal artery is tender and permanently visibly thickened, tortuous and sometimes nodular; excision of the affected segment of the temporal artery often relieves the pain (Horton, Magath and Brown, 1934; Cooke, Cloake, Govan and Colbeck, 1946; Kilbourne and Wolff, 1946).

Trigeminal neuralgia is distinguished from migraine in the trigeminal area by the presence of 'trigger zones' and the occurrence of pain along the lips and tongue.

Histamine cephalgia (Horton, 1941) is associated with lacrimation and congestion of the eye, eyelids and nose on the affected side and is not accompanied by visceral disturbances.

Temporal, occipital and supraorbital neuralgias may be occasionally misdiagnosed as migraine (Harris, 1937).

Aniseikonia may occasionally be mistaken for a migrainous aura (Bannon, 1940).

Epilepsy may be mistakenly suspected because of the presence of an aura, but the momentary duration of the epileptic aura as opposed to the several minutes' duration of the migrainous aura and, moreover, the absence of any disturbances of consciousness in migraine should be sufficient to indicate the correct diagnosis on the history alone.

Prognosis

Though the condition may last a lifetime it is not dangerous to life and tends to disappear spontaneously after the natural, but not the artificial, menopause or the age of about 50. As far as frequency of the attacks and their severity are concerned, these may be considerably improved by treatment.

Treatment

No treatment is really specific, as can be inferred from the number of drugs and procedures that have been used. They may be considered under the following headings:—

(A) PROPHYLACTIC

In the period between attacks:—

1. Great attention must be paid to the regulation of the patient's mode of life (Fothergill, 1784). The most favourable hygienic conditions, including a carefully regulated and supervised diet, prevention of constipation, correction of anaemia, avoidance of excitement and worry, exercise without exhaustion, a congenial occupation and exemption from excessive brain work, are often helpful in reducing the frequency and severity of the attacks (Minot, 1923; Kerppola, 1926; Schnabel, 1928; Barborka, 1929; Goldzieher and Popkin, 1946). In the case of allergy to food special attention must be paid to the diet.

2. Errors of ocular refraction and/or muscle balance must be corrected by suitable spectacles or exercises, and in the opinion of Hurst (1924) this suffices to cure many sufferers.

3. The most valuable drug, if taken regularly over many months, is *phenobarbitone*, an adequate dose being $\frac{1}{2}$ gr. three times a day (Soltz *et al.*, 1935).

4. A prolonged course of *bromides* or of *cannabis indica* is sometimes effective (Carron de la Carrière, 1905).

5. In hypertensive subjects a course of *nitroglycerin* may be useful (Gowers, 1907).

6. *Potassium thiocyanate* (3 to 6 gr. daily) has been effective in keeping free from migraine both in hypertensive subjects and those with a normal blood pressure (Barker, Lindberg and Wald, 1941; Engle and Evanson, 1942; Hines and Eaton, 1942).

7. Intravenous injection of 0.5 or 1 gm. of *sodium thiosulphate* twice a week for 12 weeks has been of benefit in a few cases.

8. When the migrainous attacks coincide with the catamenia, administration of an *oestrogen* (best given as *stilboestrol* 0.5 mgm. daily in the week preceding the expected date of the next period) may be given with profit.

9. When the attacks are pre-menstrual or menstrual, *testosterone propionate* (30 to 150 mgm.) has helped on occasions (Friedman, Brenner and Merritt, 1946).

10. Various *hormones* (*ovarian, placental and pituitary*) have been tried, the most favourable reports suggesting that not more than 7 per cent. of all patients thus treated are improved (Brown, 1929; Blakie and Hossack, 1932; Egglestone and Weiss, 1932; Henriksen, 1933; Riley, Brickner and Kurzrok, 1933; Brock, O'Sullivan and Young, 1934; Soltz *et al.*, 1935; Glass, 1936; Moffat, 1937; Dunn, 1941; von Storch, 1941; Trowbridge, von Storch and Moore, 1942; Leyton, 1944; Alvarez, 1947).

11. *Thyroid extract* has been given (Moehlig, 1931).

12. *Bile salts* by mouth have been used by Hunt (1933) with success.

13. *Chondroitin-sulphuric acid* (4 gm. daily) has relieved some patients from attacks (Crandall, Roberts and Snorf, 1936; Drewyer, 1940).

14. *Reduction of fluid intake* to 1 qt. a day is often successful (McQuarrie, 1932; Kennedy, 1946).

15. *Urea* (1.3 to 4. gm. a day) has relieved some patients from attacks (Brown, 1943).

16. In an attempt to mobilize extracellular fluid thus compensating and inhibiting fluctuations in the circulating blood volume, a mixture of *calcium lactate* and *potassium chloride* has been used (Pfeiffer *et al.*, 1943).

17. 'Desensitization' with *prostigmin* (Pelner and Aibel, 1942; Pelner, 1943; Patton, 1946) or *histamine* (Butler and Thomas, 1945; Horton and Macy, 1946) have been favourably reported on.

18. Oral *carbachol* (2 mgm. three times a day) has been enthusiastically recommended by James (1945).

19. *Vitamin B₁*, usually given as *thiamine chloride* (30 to 100 mgm. daily for four weeks, followed by a maintenance dose varying from 30 mgm. once a week to 100 mgm. three times a week) has been stated to have given good results in 65 per cent. of a large series of cases (Palmer, 1945).

20. *Autohaemotherapy* has been tried (Durand, 1921).

21. *Theophylline* (9 gr. daily) has been advised (Marin, 1946).

22. *Benadryl* has been successful on occasions (Gottlieb, 1942; Friedman, Brenner and Merritt, 1946; Alvarez, 1947).

23. Oral *dihydro-ergotamine* (1 to 2 mgm. two or three times a day indefinitely) lessens the frequency and severity of the attacks and may inhibit them altogether (Bartstra, 1946; Pollock, 1946; Spuehler, 1946; Chapuis, 1948; Kral, 1948). No side effects have been observed with this dosage.

24. A *galvanic ring*, if worn constantly, may prevent the occurrence of attacks (personal observation), probably by subconscious auto-suggestion.

(B) SYMPTOMATIC

During an attack:—

(a) General measures:—

The patient should be kept absolutely quiet in bed in a darkened room, and alkaline fluids should be given freely by mouth.

Local application of cold to the head is always welcome and may relieve the pain in the less severe cases. A tight headband (Schumacher, Ray and Wolff, 1940; Sutherland and Wolff,

1940) or holding the breath for two minutes (Freeman, 1946) reduces the intensity of the headache.

If the symptoms appear at the end of an exhausting day, a good meal and a glass of good wine will sometimes abort an attack provided nausea has not set in. Strong hot coffee may give relief if the patient feels faint and nauseated.

Sodium amytal by mouth or by injection (1 to 7½ gr.) is often useful in giving comfort. A rectal suppository of *nembutal* (2 or 3 gr.) is a good adjuvant treatment, especially if nausea and vomiting are troublesome. Lavage of the stomach with water at 105° F. (40.5° C.), a brisk saline cathartic and irrigation of the colon with saline solution are sometimes of value at the onset.

If vomiting is severe, rectal infusion of 5 per cent. glucose shortens the attack and lessens the subsequent exhaustion.

(b) Obsolescent 'specific' measures:—

1. Sir Lauder Brunton (1894) recommended sodium salicylate 15 gr. and potassium bromide 30 gr. at the onset.

2. *Calcium lactate*, 30 gr., if given at the very onset may abort an attack (Bigland, 1923; Riggs, 1926).

3. *Acetyl-salicylic acid* is sometimes effective in doses of 5 to 20 gr., with or without the addition of 5 gr. of *caffeine citrate*, when given at the onset and repeated in one hour (Wolff, Hardy and Goodell, 1941).

4. An intravenous injection of *ascorbic acid* (0.5 to 1 gm.) will terminate many headaches (von Storch, 1947) including migraine.

5. Inhalation of 7 l. per minute of pure *oxygen* for periods from 30 minutes to 2 hours has been very favourably reported on (Cobb and Fremont-Smith, 1931; O'Sullivan, 1936; Alvarez and Mason, 1940; Rémond, Davies and Bronk, 1946).

6. *Butyl chloral-hydrate*, up to 4 gr., given either alone or with *Tinct. Gelsemii* 20 minims and/or *Tinct. Cannabis indica* 15 minims, may afford relief.

7. *Adrenalin* (0.6 ml. of a 1/1000 solution) given subcutaneously, may be useful if administered at the onset but is contraindicated in the presence of hypertension.

8. Lumbar puncture (Mingazzini, 1917), intravenous *sodium bicarbonate* (Sicard, Paraf and Forestier, 1921), intravenous *hypertonic saline* (Villey and Buvat, 1937) and *intravenous glucose* have all successfully aborted attacks in a few patients.

9. Intravenous injection of *peptone* has helped some patients (Auld, 1920; Miller and Raulston, 1923; Ball, 1927; Brown, 1929).

10. Intravenous injection of 3 to 30 mgm. of

amphetamine sulphate at the rate of 1 mgm. per minute has been successful in stopping a developing attack in a small group of cases (Gottlieb, 1942).

11. Intramuscular injection of 100 mgm. of *methyl-iso-octenylamine hydrochloride* (repeated in two hours if necessary) is said to have terminated attacks in occasional patients (Palmer, 1945; Friedmann, Brenner and Merritt, 1946; MacNeal and Davis, 1947).

12. Even *insulin shock* has been advised (Tillim, 1944) to stop severe attacks.

(c) Recent 'specific' measures:—

1. A large dose of *nicotinic acid* (100 to 200 mgm. intravenously) benefits patients in whom arterial spasms occur during the attack (Enrique, 1943; Atkinson, 1944; Goldzieher and Po pkin, 1946).

2. *Ergotamine tartrate* by mouth (or better dissolved under the tongue) in doses of 2 mgm. (repeated hourly if necessary up to a total of 10 mgm.) is often effective, particularly if given early in the attack; it may cause vomiting (prevented by *atropine sulphate* 1/100 gr.) and should be used with caution in vascular diseases. It may be given also by subcutaneous or intramuscular injection in doses of 0.25 to 0.5 mgm. every 2 or 3 hours till the headache ceases. It is dangerous if injected intravenously, and should not be given during menstruation (as it has a powerful uterotonc action). It is definitely contraindicated in pregnancy, hepatitis, obliterative vascular disease and in renal disorders (Brock, O'Sullivan and Young, 1934; Lennox and von Storch, 1935; van der Scheer, 1938; von Storch, 1941).

3. *Dihydro-ergotamine* injected subcutaneously or intramuscularly in doses of 0.5 to 3 mgm. (repeated in 1 or 2 hours if necessary in severe and persistent attacks) successfully terminates migrainous attacks within 2 hours of administration in 80 to 90 per cent. of patients; the effect is most pronounced and most rapid if it is exhibited early in the attack. In the absence of nausea and vomiting and in mild attacks 1 to 2 mgm. by mouth (repeated up to three times daily) may be effective. Intravenous injection (not more than 0.5 mgm.) may be given in very exceptional cases, but is not recommended as it may result in vertigo and precordial pain as well as in exacerbation of the headache, nausea and vomiting. It has no effect on the uterine musculature and is not contraindicated in pregnancy or in vascular disease. Occasionally, especially if used in high dosage late

in an attack, it may cause nausea and vomiting (effect inhibited by *atropine sulphate*, 1/100 gr.) (Ekbohm, 1944; Hartman, 1945; Horton, Peters and Blumenthal, 1945; Friedman and Friedman, 1945; Allan, 1946; Clein, 1946; Dannenberg, 1946; Spuehler, 1946; Alvarez, 1947; Blumenthal and Fakler, 1947; Dreyfus, 1947; Friedman and Wilson, 1947; von Storch, 1947; Tillgren, 1947; Chapuis, 1948).

4. If the pain is unusually severe *morphia* $\frac{1}{2}$ gr. or *pethidine hydrochloride* 200 mgm. may be necessary.

(C) SURGICAL TREATMENT

1. In a few selected cases of atypical migraine affecting chiefly one eye, temple and upper part of the cheek, sometimes producing lacrimation and congestion of the eyeball, temporary or permanent relief may be obtained by alcohol injection of the Gasserian ganglion (Harris, 1946).

2. Injection of procaine into or ligation, section or resection of the temporal (Nadler, 1945; Patzer, Derbes and Engelhardt, 1945; Frouchtman, 1945; Freeman, 1946; Moore, 1946), supra-orbital (Freeman, 1946; Moore, 1946) and/or occipital (Freeman, 1946) arteries has been successful in aborting and inhibiting attacks; unfortunately the effect is usually only transient and rarely lasts for more than one year (von Storch, 1947).

3. The middle meningeal artery has been ligated (Dickerson, 1933).

4. A periarterial sympathectomy of the external and internal carotid arteries close to the base of the skull has been performed (Hellwig, 1924).

5. Removal of the inferior cervical and first thoracic sympathetic ganglia has been reported (Dandy, 1931).

6. Rowbotham (1946) has successfully performed a periarterial sympathectomy of the common, internal and external carotid arteries together with division of the external carotid artery and simultaneous removal of the lower half of the superior cervical sympathetic ganglion.

7. Finally, even sub-temporal decompression has been carried out in excessively severe cases (Buchanan, 1924; Alvarez, 1947).

The writer wishes to thank Dr. S. P. Meadows, F.R.C.P., for attracting his attention to the subject, and Miss Irene Colbert, M.B., Mr. G. F. Home, Miss W. C. Donkin and Mr. T. Bradbeer for their courtesy and help in obtaining, collecting and checking references.

BIBLIOGRAPHY

- ALLAN, F. M. (1946), *Lahey Clin. Bull.*, 5, 52.
ALVAREZ, W. C. (1940), *Proc. Staff Meet. Mayo Clin.*, 15, 380.
ALVAREZ, W. C. (1947), *Gastroenterology*, 9, 754.

- ALVAREZ, W. C., and MASON, A. Y. (1940), *Proc. Staff Meet. Mayo Clin.*, 15, 616.
ATKINSON, M. (1943), *Ann. Int. Med.*, 18, 797.

- ATKINSON, M. (1944), *Ann. Int. Med.*, 21, 990.
- AULD, A. G. (1920), *Brit. Med. J.*, 1, 567.
- BAKER, B. M. (1940), *Tr. A. Am. Physicians*, 55, 294.
- BALL, F. E. (1927), *Am. J. Med. Sc.*, 173, 781.
- BANNON, R. E. (1940), *Am. J. Optometry*, 17, 1501.
- BARBORKA, C. J. (1929), *M. Clin. N. Amer.*, 12, 1639.
- BARBORKA, C. J. (1930), *J. Am. Med. Ass.*, 95, 1825.
- BARKER, M. H., LINDBERG, H. A., and WALD, M. H. (1941), *J. Am. Med. Ass.*, 117, 1591.
- BARTSTRA, H. K. G. (1946), *Ned. Tijdschr. Geneesk.*, 90, 1786.
- BARUK, H. (1931), *Encéphale*, 26, 42.
- BASSOE, P. (1933), *J. Am. Med. Ass.*, 101, 599.
- BIGLAND, A. D. (1923), *Brit. Med. J.*, 11, 1133.
- BLAKIE, N. H., and HOSSACK, J. C. (1932), *Canad. M. A. J.*, 27, 45.
- BLUMENTHAL, L. S., and FAKLER, B. (1947), *Med. Ann. D. C.*, 16, 10.
- BRAMS, W. A. (1922), *J. Am. Med. Ass.*, 78, 26.
- BRAVAIS, L. F. (1827), 'Recherches sur les symptômes et le traitement de l'épilepsie hémiplegique,' Thèse No. 118, Paris.
- BROCK, S., O'SULLIVAN, M., and YOUNG, D. (1934), *Am. J. M. Sc.*, 188, 253.
- BROWN, J. A. (1943), *Brit. Med. J.*, 11, 201.
- BROWN, T. R. (1921), *J. Am. Med. Ass.*, 77, 1396.
- BROWN, T. R. (1920), *Tr. A. Am. Physicians*, 44, 215.
- BRUGELMANN, W. (1909), 'Die Migräne,' Wiesbaden.
- BRUNTON, T. L. (1894), *Practitioner*, 52, 101.
- BUCHANAN, J. A. (1920), *Med. Rec.*, 98, 807.
- BUCHANAN, J. A. (1924), *S. G. O.*, 38, 638.
- BUTLER, S., and THOMAS, W. A. (1945), *J. Am. Med. Ass.*, 128, 173.
- CARMICHAEL, F. A. (1943), *J. Kansas M. Soc.*, 44, 333.
- CARRON DE LA CARRIÈRE, G. (1905), *Medecin Brux.*, 15, 305.
- CHAPUIS, J. P. (1948), *Schweiz. Med. Wschr.*, 78, 1125.
- CHIRAY, M., and TRIBOULET, F. (1925), *Presse Med.*, 33, 313.
- CLEIN, N. W. (1946), *Ann. Allergy*, 4, 128.
- COBB, S., and FREMONT-SMITH, F. (1931), *Arch. Neurol. and Psychiat.*, 26, 731.
- COOKE, W. T., CLOAKE, P. C. P., GOVAN, A. D. T., and COLBECK, J. C. (1946), *Quart. J. Med.*, 15, 47.
- CRANDALL, L. A., and ROBERTS, G. M. (1933), *Illinois M. J.*, 63, 513.
- CRANDALL, L. A., and ROBERTS, G. M. (1933), *Proc. Soc. Exper. Biol. and Med.*, 30, 704.
- CRANDALL, L. A., ROBERTS, G. M., and SNORF, L. D. (1936-1937), *Am. J. Digest. Dis.*, 3, 289.
- CRITCHLEY, M., and FERGUSON, F. R. (1933), *Lancet*, 1, 123 and 182.
- CURSCHMANN, H. (1939), *Handbuch d. Inn. Med.*, 5, 1505.
- DANDY, W. E. (1931), *Bull. Johns Hopkins Hosp.*, 48, 357.
- DANNENBERG, TH. (1946), *Perm. Found. Med. Bull.*, 4, 96.
- DERBES, V. J., ENGELHARDT, H. T., and WATTERS, T. A. (1945), *South M. J.*, 38, 533.
- DIAMOND, J. S. (1927), *Am. J. M. Sc.*, 174, 695.
- DIAMOND, J. S. (1934), *M. Rec.*, 139, 634.
- DICKERSON, D. G. (1933), *J. Nerv. and Ment. Dis.*, 77, 42.
- DREYER, G. E. (1940), *J. Michigan M. Soc.*, 39, 486.
- DREYFUS, PH. R. (1947), *Rev. Med. Suisse Rom.*, 67, 122.
- DUNN, C. W. (1941), *Delaware State M. J.*, 13, 89.
- DURAND, G. (1921), *Bull. gen. de Therap. Paris*, 172, 159.
- EGGLESTON, C., and WEISS, S. (1932), *Am. J. M. Sc.*, 183, 283.
- EKBOM, K. A. (1944), *Nord. Med.*, 22, 861.
- ENGLE, D. E., and EVANSON, C. O. (1942), *Am. J. M. Sc.*, 204, 697.
- ENRIQUE, E. (1943), *Rev. Clin. Espan.*, 10, 53.
- ESCHBACK, H. (1927), 'Epilepsie und Migräne,' Bonn.
- FABRE, E. (1904), 'La Migraine chez les enfants.'
- FITZ-HUGH, T. (1940), *Intern. Clinics*, 1, 143.
- FLATAU, E. (1912), 'Die Migräne,' Berlin.
- FOTHERGILL, J. (1784), 'Medical Observations and Enquiries,' 6, 103.
- FREEMAN, W. (1946), *J. Am. Med. Ass.*, 132, 501.
- FRIEDLANDER, W., and PETOW, I. (1927), *Med. Klin.*, 23, 1498.
- FRIEDMAN, A. P., and BRENNER, C. (1945), *N. York State J. Med.*, 45, 1969.
- FRIEDMAN, A. P., BRENNER, C., and MERRITT, H. H. (1946), *J. Am. Med. Ass.*, 132, 498.
- FRIEDMAN, M. D., and FRIEDMAN, D. A. (1945), *Ohio State Med. J.*, 41, 1099.
- FRIEDMAN, M. D., and WILSON, E. J. (1947), *Ohio Med. J.*, 43, 934.
- FROUCHTMAN, R. (1945), *Med. Clin. Barcelona*, 4, 396.
- GÄNSSLEN, M. (1921), *Med. Klin. Berl.*, 17, 1232.
- GLASS, S. J. (1936), *Endocrinology*, 20, 333.
- GOLDZIEHER, J. W., and POPKIN, G. L. (1946), *J. Am. Med. Ass.*, 131, 103.
- GOTTLIEB, J. S. (1942), *Am. J. M. Sc.*, 204, 553.
- GOWERS, W. R. (1907), 'Borderland of Epilepsy, Faints, Vagal attacks, Vertigo, Migraine, Sleep symptoms and their Treatment,' London.
- GRIMES, E. (1931), *Med. J. and Rec.*, 134, 417.
- HARRIS, W. (1937), 'The Facial Neuralgias,' London.
- HARRIS, W. (1946), *Brit. Med. J.*, 1, 754.
- HARTMAN, M. D. (1945), *Ann. Allergy*, 3, 440.
- HAUG, H., and WOHRMANN, W. (1930), *Deut. Med. Woch.*, 26, 1085.
- HELLWIG, A. (1924), *Arch. f. Klin. Chir.*, 128, 261.
- HELLWIG, A. (1924), *J. Am. Med. Ass.*, 82, 1086.
- HENRIKSEN, K. Z. (1933), *Acta Psychiat. and Neurol.*, 8, 701.
- HINES, E. A., and EATON, L. M. (1942), *Proc. Staff Meet. Mayo Clin.*, 17, 254.
- HIRSCH, B. R. (1765), 'Paris Quinti Nervorum Encephali Disquisitio Anatomica,' Vienna.
- HORTON, B. J., MAGATH, T. B., and BROWN, G. E. (1934), *Arch. Int. Med.*, 53, 400.
- HORTON, B. T. (1941), *J. Am. Med. Ass.*, 116, 377.
- HORTON, B. T., and MACY, D. (1946), *M. Clin. N. Am.*, 30, 811.
- HORTON, B. T., PETERS, G. A., and BLUMENTHAL, L. S. (1942), *Proc. Central Soc. Clin. Res.*, 15, 91.
- HORTON, B. T., PETERS, G. A., and BLUMENTHAL, L. S. (1945), *Proc. Staff Meet. Mayo Clin.*, 20, 241.
- HORTON, B. T., PETERS, G. A., and BLUMENTHAL, L. S. (1947), 'Festschrift Prof. Stoll,' Benno Schwabe, Basel, p. 355.
- HUNT, T. C. (1933), *Lancet*, 11, 279.
- HURST, A. F. (1924), *Lancet*, 11, 3.
- HYSLIP, G. H. (1934), *M. Clin. N. Am.*, 18, 827.
- JACKSON, J. H. (1863), *Med. Times and Gaz.*, 1, 588.
- JAMES, A. K. (1945), *Brit. Med. J.*, 1, 663.
- KENNEDY, F. (1946), *J. Am. Med. Ass.*, 132, 502.
- KERPOLA, W. (1926), *Monatschr. f. Psychiat. u. Neurol.*, 61, 83.
- KILBOURNE, E. D., and WOLFF, H. G. (1946), *Ann. Int. Med.*, 24, 1.
- KRAL, V. A. (1948), *Schweiz. Arch. Neurol. Psychiat.*, 62, 128.
- LENNOX, W. G. (1941), 'Science and Seizures,' New York.
- LENNOX, W. G., and VON STORCH, T. J. C. (1935), *J. Am. Med. Ass.*, 105, 169.
- LEYTON, N. (1944), *M. Press*, 211, 302.
- LIVENIG, E. (1873), 'On Megrim, Sick Headache and some Allied Disorders.'
- LYON, G. (1920), *Bull. Med.*, 43, 1145.
- MCCLURE, C. W., and HUNTSINGER, M. E. (1928), *New Eng. J. Med.*, 199, 1312.
- MACNEAL, P. S., and DAVIS, D. (1947), *Ann. Int. Med.*, 26, 526.
- MCQUARRIE, I. (1932), *Ann. Int. Med.*, 6, 497.
- MANGELSDÖRF, F. (1903), *Berl. Klin. Wchschr.*, 40, 1004.
- MARIN, R. B. (1946), *J. M. Soc. N. Jersey*, 43, 274.
- MENDEL, G. H. (1866), *Verhandl. d. Naturf. Vereins in Brunn.*, 4, 3.
- MILLER, J. L., and RAULSTON, B. O. (1923), *J. Am. Med. Ass.*, 80, 1894.
- MINGAZZINI, G. (1917), *Policlin. Roma*, 24, 269.
- MINOT, G. R. (1923), *M. Clin. N. Am.*, 7, 715.
- MÖBIUS, P. J. (1894), 'Die Migräne.'
- MOEHLIG, R. C. (1931), *Endocrinology*, 15, 11.
- MOENCH, L. G. (1947), 'Headache,' Chicago.
- MOFFATT, W. M. (1937), *J. Am. Med. Ass.*, 108, 612.
- MOLONEY, J. C. (1928), *Arch. Neurol. and Psychiat.*, 19, 684.
- MONRO TERTIUS, A. (1825), 'Elements of Anatomy of the Human Body,' 2, 363.
- MOORE, M. T. (1946), *J. Am. Med. Ass.*, 132, 502.
- MORENAL, L., and DÉCHAUME, J. (1929), *J. Med. Lyon*, 10, 259.
- MORLOCK, C. G., and ALVAREZ, W. C. (1940), *J. Am. Med. Ass.*, 114, 1744.
- NADLER, S. B. (1945), *J. Am. Med. Ass.*, 129, 334.
- O'SULLIVAN, M. E. (1936), *J. Am. Med. Ass.*, 107, 1208.
- PALMER, H. D. (1941), *Arch. Neurol. and Psychiat.*, 45, 368.
- PALMER, H. D. (1945), *Clinics*, 4, 531.
- PATTON, I. J. (1946), *Canad. M. A. J.*, 54, 588.
- PATZER, R., DERBES, V., and ENGELHARDT, H. (1945), *Arch. Surg.*, 50, 296.
- PELNER, L. (1943), *Dis. Nerv. System*, 4, 177.
- PELNER, L., and AIBEL, M. E. (1942), *J. Lab. and Clin. Med.*, 27, 1546.
- PFEIFFER, C., DREISBACH, R. H., and ROBY, C. C. (1944), *J. Lab. and Clin. Med.*, 29, 709.
- PFEIFFER, C., DREISBACH, R. H., ROBY, C. C., and GLASS, H. G. (1943), *J. Lab. and Clin. Med.*, 28, 1219.
- POLLOCK, L. A. (1946), *Rosky Mountain M. J.*, 13, 895.
- POUSSEPP, D. (1925), *Rev. Neurol.*, Paris, 32, 925.
- RAY, B. S., and WOLFF, H. G. (1940), *Arch. Neurol. and Psychiat.*, 41, 813.
- REMOND, A., DAVIES, P. W., and BRONK, D. W. (1946), *Fed. Proc.*, 5, 86.
- RIGGS, C. E. (1926), *Minnesota Med.*, 9, 87.
- RILEY, H. A. (1932), *Bull. Neurol. Inst. N. York*, 2, 429.
- RILEY, H. A., BRICKNER, R. M., and KURZROK, R. (1933), *Bull. Neurol. Inst. N. York*, 3, 53.
- BOWBOTHAM, G. F. (1942), *Brit. Med. J.*, 11, 685.
- ROWBOTHAM, G. F. (1946), *Brit. Med. J.*, 11, 319.
- VAN DER SCHEER, W. M. (1938), *Ned. Tijdschr. Geneesk.*, 82, 5843.
- SCHNABEL, T. G. (1928), *Ann. Int. Med.*, 2, 341.
- SCHUMACHER, G. A., RAY, B. S., and WOLFF, H. G. (1940), *Arch. Neurol. and Psychiat.*, 44, 701.
- SCHUMACHER, G. A., and WOLFF, H. G. (1941), *Arch. Neuro. and Psychiat.*, 45, 199.
- SICARD, J. A., PARAF, J., and FORESTIER, J. (1921), *Bull. et Mem. Soc. Med. Hop. Paris*, 15 (3rd S.), 1204.

- SIMONS, D. J., DAY, E., GOODELL, H., and WOLFF, H. G. (1943), *Research Publ. A. Nerv. and Ment. Dis.*, **23**, 228.
- SINKLER, W. (1887-88), *Maryland Journal*, **18**, 1.
- SLATER, J. K. (1948), *Edinb. Med. J.*, **55**, 173.
- SMITH, C. B. (1946), *Canad. M. A. J.*, **54**, 589.
- SOLTZ, S. E., BRICKNER, R. M., RILEY, H. A., and SALMON, L. A. (1935), *Bull. Neurol. Inst. N. York*, **4**, 432.
- SPITZER, A. (1901), 'Ueber Migräne,' Jena.
- SPUEHLER, O. (1946), *Schweiz. Med. Wschr.*, **76**, 1259.
- VON STORCH, T. J. C. (1937), *Nervenarzt*, **10**, 469.
- VON STORCH, T. J. C. (1937), *New Eng. J. Med.*, **217**, 247.
- VON STORCH, T. J. C. (1938), *J. Am. Med. Ass.*, **111**, 293.
- VON STORCH, T. J. C. (1941), *Med. Clin. N. Am.*, **25**, 1317.
- VON STORCH, T. J. C. (1947), *Amer. Practit.*, **1**, 631.
- SUTHERLAND, A. M., and WOLFF, H. G. (1940), *Arch. Neurol. and Psychiat.*, **44**, 929.
- THOMAS, W. A., and BUTLER, S. (1946), *Am. J. Med.*, **1**, 39.
- THOMAS, W. A., and BUTLER, S. (1946), *Bull. N. York Acad. Med.*, **22**, 125.
- TILLGREN, N. (1947), *Nord. Med.*, **33**, 502.
- TILLGREN, N. (1947), *Nord. Med.*, **34**, 937.
- TILLGREN, N. (1947), *Acta Med. Scand. (Suppl.)*, **196**, 222.
- TILLIM, S. J. (1944), *Ann. Int. Med.*, **20**, 597.
- TODD, R. B. (1854), 'Clinical Lectures on Paralysis, Diseases of the Brain and Other Affections of the Nervous System,' London, p. 281.
- TORDA, C., and WOLFF, H. G. (1945), *Arch. Neurol. and Psychiat.*, **53**, 329.
- TROWBRIDGE, L. S., VON STORCH, T. J. C., and MOORE, M. (1942), *New Eng. J. Med.*, **227**, 699.
- UNGER, L. (1940), *J. Allergy*, **12**, 197.
- VALLERY-RADOT, P., and BLAMOUTIER, P. (1927), *Bull. et Mem. Soc. Med. Hop. Paris*, **51**, 925.
- VILLEY, G., and BUVAT, J. F. (1937), *Paris Med.*, **103**, 189.
- VON WASSERMAN, A., NEISSER, A., and BRUCK, C. (1906), *Dtsch. Med. Wchschr.*, **32**, 745.
- WEISMANN, S. (1924), 'Des Migraines,' Paris.
- WHITEHEAD, R. W., and MCNIEL, E. E. (1935), *Am. J. Psychiat.*, **91**, 1275.
- WHITEHORN, J. C. (1944), *Arch. Neurol. and Psychiat.*, **52**, 197.
- WILSON, D. C. (1925), *Clifton M. Bull.*, **11**, 71.
- WOLFF, A. A., and UNGER, L. (1944), *Ann. Int. Med.*, **20**, 828.
- WOLFF, H. G. (1940), 'Modern Medical Therapy in General Practice,' Baltimore.
- WOLFF, H. G. (1948), 'Headache and other Head Pain,' New York.
- WOLFF, H. G., HARDY, J. D., and GOODELL, H. (1941), *J. Clin. Invest.*, **20**, 63.

INFECTIONS OF THE FEET IN DIABETES

With Special Reference to Those Due to Gas-Forming Organisms

By E. C. B. BUTLER, F.R.C.S.

The London Hospital

It is a common error to regard all infections of the feet occurring in diabetic patients as cases of incipient gangrene. Most of these patients can be safely treated at home or in the out-patient department. Only a minority need admission to hospital, and of these only a small proportion have true necrosis or require a major amputation. The incidence of severe infection has been much reduced since the introduction of penicillin.

Patients who require in-patient treatment may for convenience be divided into two groups, although the dividing line between the two is often difficult to determine.

Group 1 consists of those patients who have signs and symptoms of senile obliterative arterial disease. The diabetic cases differ only in having infection as a constant feature.

Group 2 consists of cases of diabetes complicated by infection of the feet, the circulation being good, the popliteal pulse being readily felt and oscillometer tests showing good pulsation below the knee.

Group 1

Following mild trauma an infection starts on one or more toes and similar lesions may arise on the heel or elsewhere on the foot. Under favourable circumstances and treatment the infection will

resolve but in other instances it may spread or go on to necrosis, which in turn may remain localized or involve the remainder of the foot.

When spread of the infection occurs there is little local reaction; formation of pus is unusual and there is no definite line of demarcation between diseased and healthy tissue. On examination, these patients are likely to show signs of thrombosis in the femoral or popliteal vessels. Popliteal pulsation is absent, oscillometer readings show minimal or absent records below the knee and the limb rapidly becomes blanched when elevated. Radiography may reveal widespread medial calcification of the main vessels.

Treatment

The patient is best treated as an in-patient. A swab from the infected area is sent to the laboratory so that the invading organisms can be identified and their sensitivity established.

Staphylococcus aureus and haemolytic and non-haemolytic streptococci are commonly found; but gram-negative bacilli may also occur. Not infrequently various types of anaerobic organisms are present and these may cause serious spreading infections. Some of these organisms are penicillin resistant and it is a wise precaution to learn without delay what drug or combination of drugs is