a week of the operation. G. D. was called in consultation to see this case. She was the *propositus* of this genealogical study.

IV 163.—A married woman, died aged 24, Durban (1950). For three years before her death she had complained greatly of abdominal pains. On two occasions she was treated as a case of pyelitis because she passed a red-coloured urine. An abortion occurred in 1947, and five months before her death she gave birth to a live child. During and after pregnancy she suffered from severe attacks of abdominal pain; she frequently vomited and was very constipated. She lost a great deal of weight. She was in a very nervous state and was taking barbiturate sedatives. Six weeks before her death it was noticed that her urine was "port wine in colour." As her symptoms were becoming worse she was admitted to hospital, where a generalized paralysis of lower motor neurone type developed. She was treated with deoxycortone acetate and ascorbic acid. After a week of almost complete paralysis she died. The details about her history were obtained from her mother and the family doctor.

IV 165.—A married woman, aged 24, acute porphyria (1954). During her 20th year she suffered from extreme nausea early in her first pregnancy, but continued to full term and gave birth to a live child. Two years later she was treated for lower abdominal pain and the cervix was cauterized. Eight months later there was an episode of epigastric pain with vomiting. Although her mother's (III 58) urine was negative when first tested for porphyrin, her urine contained an excess of porphyrin and she was warned in writing that she was a porphyric. The danger of drugs was emphasized. Seven months after this, believing herself again pregnant, she took certain drugs. She developed extreme nausea and vomiting, with abdominal pain. Constipation was marked. She became acutely ill and was fed intravenously. Her urine was reddish brown in colour, and when examined contained a great excess of porphyrin and porphobilinogen. At this stage her skin was very sensitive and abraded very easily. There was weakness of her limbs, but no true paralysis. The symptoms slowly subsided and she was discharged from hospital after three weeks.

Summary

The family tree from a large porphyric family group is presented. This group is typical of twelve others that have been investigated. In all these groups porphyria has appeared in its acute form, in its chronic cutaneous form (the "cutanea tarda" type), or as a symptomless porphyrinuria. In many cases one type changed into the other. They are different manifestations of the same inherited disorder.

It is shown that 50% of the children of a porphyric parent will inherit porphyria and that the distribution of the inheritance between the sexes is approximately equal. That is, porphyria as it occurs in South Africa is inherited as a Mendelian dominant characteristic and is not sex-linked.

If porphyria is inherited, cutaneous manifestations are more pronounced in men and are often very slight and infrequent in women. On the other hand, acute attacks are common in women. The reason for this is not fully understood. Men are more constantly exposed to the sun and to trauma; women appear more likely to be given sedative drugs or to be operated on for abdominal pain, often under a barbiturate anaesthetic. There may also be endocrine factors.

In the latent stage diagnosis may be difficult. The personal and family history is of the utmost importance, and the urine and faeces should be examined by a biochemist who is experienced in detecting porphyrins.

When a case of porphyria is diagnosed it is important to trace the genealogical tree and to investigate the other

members of the family group. These investigations will usually result in the discovery of many other cases who could then be warned of the inherent danger.

We would like to express our appreciation to Mrs. C. van der Walt, who undertook the vast correspondence involved in this research; to Dr. K. van der Walt, who was responsible for the family tree; and to Dr. J. A. Fraser Roberts for advice about the final draft. Our thanks are also due to Dr. F. W. K. Grotepass, of Pretoria University, and all the other doctors in South Africa, Europe, and America who have given us their co-operation.

REFERENCES

- Barnes, H. D. (1951). *S. Afr. J. clin. Sci.*, 2, 117.
Cockayne, E. A. (1933). *Inherited Abnormalities of the Skin and its Appendages*. Oxford Univ. Press, London.
Dean, G. (1953). *British Medical Journal*, 2, 1291.
Rimington, C. (1952). Second International Congress of Biochemistry. Paris.
Waldenström, J. (1937). *Acta med. scand.*, Suppl. 82.
— and Vahlquist, B. (1944). *Ibid.*, 117, 1.
Watson, C. J. (1952). *Diseases of Metabolism*, 3rd ed., edited by G. G. Duncan. Philadelphia.
Wells, G. C., and Rimington, C. (1953). *Brit. J. Derm.*, 65, 337.

QUININE AMBLYOPIA

TREATMENT BY STELLATE GANGLION BLOCK

BY

LOUIS GLICK, M.D., M.R.C.P.

Physician, Royal Halifax Infirmary

AND

JOYCE MUMFORD, M.B., B.S.

House-Physician, Royal Halifax Infirmary

Quinine, which was discovered more than 300 years ago, has proved of inestimable value in the treatment of malaria. It has played a lesser part in the treatment of muscular dystrophies. It has frequently been incorporated in proprietary and home-made antifebrile mixtures and tonic wines. Its use as an abortifacient has been reported on several occasions.

In susceptible people a dose as small as 1 gr. (65 mg.) may produce transient disturbance of vision. Permanent optic atrophy with restricted visual fields has been reported in the case of a man who drank two bottles of proprietary orange-and-quinine wine. By contrast others, especially those living in tropical climates, have taken doses of between 100 and 200 gr. (6.5 and 13 g.) daily without obvious ill effects. There has never been a satisfactory explanation for the wide range of sensitivity to this drug. Unfortunately, the sale of this potentially dangerous substance is unrestricted and the grave risk of permanent damage, especially to the visual apparatus, is insufficiently appreciated.

Case History

A married woman aged 31, knowing herself to be eight weeks pregnant and wishing to procure an abortion, purchased without difficulty $\frac{1}{2}$ oz. (15 g.) of powdered quinine sulphate at a chemist's shop. At 1 a.m. on Sunday, January 2, 1955, she dissolved the powder in a glass of port and drank the contents of the glass. Within a few minutes her vision was blurred and she experienced buzzing in her ears. She went to bed feeling very ill and in about an hour's time began to vomit. The vomiting continued repeatedly, but she eventually fell asleep. At 7 a.m. the same morning she awoke to find herself completely deaf and completely blind. She remained deaf and blind throughout that day, and by the following morning the blindness was still absolute, but the hearing had improved. She was admitted to the Royal Halifax Infirmary at 4 p.m. on January 3.

On admission she was quite rational and was able to give a full account of her activities. She was not sweating, her colour was good, and she was not in any way distressed. The pulse was 90 a minute and regular, respirations 18, and blood pressure 120/80. She was able to hear when addressed in an ordinary conversational tone. The pupils were equal, widely dilated, and fixed. Full ocular movements were retained, but she was completely blind. Extreme pallor of the optic disks and of both retinae was observed. No abnormality of note was discovered in the other systems. An electrocardiogram was normal. When seen by an ophthalmologist at 7 p.m. the complete absence of perception to light was confirmed. He noted extreme pallor of the optic disks with blurring of the edges of the disks. He also commented on the milky appearance of the retinae due to oedema, especially around the maculae. Narrowing of the retinal vessels was most obvious in the smaller branches, and the terminal twigs were invisible.

Treatment

In view of the marked vascular spasm and the observed pallor of the optic nerves and maculae, she was treated with vasodilators and intensive vitamin B intravenously. Papaverine hydrochloride 1 gr. (65 mg.) was given intravenously at once, and this was reinforced by sodium nitrite, 100 mg. intravenously. The papaverine was continued four-hourly but no further sodium nitrite was given.

At 10 p.m. "parentrovite," one pair of ampoules, was injected intravenously and thereafter six-hourly. This preparation consists of massive proportions of the total vitamin B complex together with vitamin C. At 10.30 p.m., when the blindness had been present for at least 39½ hours, and because there was no obvious improvement, bilateral stellate ganglion block was performed.

Numerous techniques are available for this procedure. Success is assured by familiarity with one method. On this occasion a high antero-lateral approach was used under local analgesia. The patient lies in a supine position with the head turned slightly toward the side opposite the one to be blocked, with a pillow under the nape of the neck. A skin weal is raised with 1% procaine two fingerbreadths above the clavicle at the level of the posterior edge of the sterno-mastoid muscle. This point is located a little below the angle formed by this muscle and the external jugular vein. The vein, if not easily seen, can be made to stand out more clearly if the patient is asked to cough whilst the nose is nipped momentarily by an assistant or by the patient himself.

The fingers of the left hand palpate the transverse processes of the cervical spine by depressing the skin in the groove behind the sterno-mastoid muscle. The most prominent bony point is the tubercle of Chassaignac, and below this lies the transverse process of the seventh cervical vertebra. A lumbar puncture needle 8-10 cm. long is inserted through the weal perpendicular to the skin, aiming for the correct sagittal bony plane, and if accurately directed comes to rest at the junction of the transverse process and the body of the seventh cervical vertebra. The ganglion lies slightly below this point, separated from the bone by the longus colli muscle. After careful aspiration, to ensure that neither a blood vessel nor the spinal canal has been accidentally punctured, 10 ml. of 1% procaine is slowly injected.

The right side was done first but without benefit. Within a minute of completing the left stellate ganglion block, and as the ptosis of the left upper lid was appearing, the patient spontaneously exclaimed, "I can see you." At that time, in a darkened ward and with only the illumination of a headlamp, she was able to count fingers with her left eye at one metre and to see faces at the foot of the bed. At this juncture we learned that since childhood she had only been able to perceive light with her right eye, owing to an extensive degree of myopia, and was wholly dependent on her left eye. This accounted for the apparent failure of the right stellate ganglion block. Though complete ptosis of the left upper lid was apparent the left pupil

remained fixed and dilated. The initial improvement was not fully maintained, and for this reason bilateral stellate ganglion block was repeated daily. The papaverine and parentrovite were continued, but were reduced to twelve-hourly injections by January 6. All treatment was suspended on January 7, the fifth day of admission. Acid sodium phosphate, 20 gr. (1.3 g.) three times daily, was given in order to facilitate excretion of quinine in the urine.

Progress

There was a notable and immediate improvement in visual acuity after each stellate ganglion block was completed, and by January 7 the patient asserted that the vision in her left eye was as good as it had ever been before, but that everything appeared dark "as though it were 4 o'clock on a winter's day." Appreciation of colour, on the other hand, for the red end of the spectrum returned early and was maintained throughout. Repeated observations of the fundi and of the visual fields were made, and at the final assessment on March 5 it was observed that the disks were still very pale, the retinal vessels still narrowed, but the oedema had disappeared. Corrected visual acuity in the left eye was 6/9. This was the same as it had been before taking the quinine. The visual field in the left eye, which had been considerably reduced, was now greatly improved, though it still showed a slight constriction at the periphery.

On January 18 vaginal examination was performed. The uterus was found to be enlarged, but smaller than expected for the estimated duration of pregnancy. It was suspected that the foetus had perished. On February 4 she passed a large blood clot spontaneously and bleeding continued per vaginam. This determined the need for evacuation of the uterus, and on February 12, under general anaesthesia, the residual products of conception were removed.

Discussion

Our experience in this case has thrown some light on the pathogenesis of quinine amaurosis. The relative roles of direct damage to nerve elements, especially the ganglion cells of the retina, and vascular spasm are still in dispute. Many authorities, including Ballantyne when discussing a case presented by King (1934-5) at the Royal Society of Medicine, have noted the appearance of amaurosis before vascular spasm could be demonstrated. Experimentally, too, in animals, damage to nerve elements has been shown to precede vascular changes. By contrast others have stressed the importance of vascular spasm. Braveman *et al.* (1948), reporting a case of quinine amblyopia, state that "the outstanding finding in the fundi was the markedly persistent vasoconstriction that led to severe retinal damage." Whatever the truth, all authorities are agreed that treatment should be directed towards producing vasodilatation. Intensive vitamin B therapy was tried in our case in addition, partly for its vasodilator effect and partly in the hope that it would reverse, or at least retard, damage to nervous tissue. Atropine, acetylcholine, and amyl nitrite have been recommended. Others, quoted by Duke-Elder (1940), have suggested paracentesis of the anterior chamber or corneo-scleral trephining.

Our own attempts to produce vasodilatation by drug therapy were ineffectual. Stellate ganglion block, on the other hand, was seen to reduce vascular spasm and to initiate an immediate return of central vision. From this it is reasonable to infer that vascular spasm was an important factor in the causation of the blindness, that it could occur early, and that it was reversible irrespective of the concurrent damage to nervous elements in the retina. Furthermore, the repeated clinical observation that the peripheral field of vision is always more seriously and more permanently affected suggests that quinine may have a selective toxic action on the rods, which are more abundant at the periphery. This view is confirmed by the fact that blue vision returned late, whereas red vision was appreciated as soon as the visual acuity improved. It is widely held that the rods are concerned with blue vision.

The capacity of stellate ganglion block to produce dilatation of cerebral vessels has been a further matter for dispute. Naffziger and Adams (1950) reported the use of this manoeuvre in a series of 155 patients suffering from acute cerebrovascular accidents together with 70 other cases suffering from a variety of cerebral disorders. Whilst admitting the difficulty of assessing the effectiveness of this measure in a disorder with such a variable response without special treatment, they conclude that their results were sufficiently gratifying to encourage its use in cases in which cerebrovascular spasm could be inferred. Leriche (1952) and Walsh (1954) have strongly advocated stellate ganglion block in the treatment of recent and late cases of cerebral thrombosis. Our experience in this case has shown that sympathetic denervation can effectively dilate the retinal arteries and by inference can dilate other cerebral arteries under control of the stellate ganglion. As a corollary it is suggested that stellate ganglion block might prove of considerable value in the treatment of other forms of retinal vascular constriction, and especially in the treatment of thrombosis of the central retinal vein and of embolism of the central retinal artery. Cotson (1951) reports a case in which stellate ganglion block was done 5½ hours after the onset of sudden blindness due to an embolus of the central retinal artery. Within fifteen minutes there was a marked dilatation of the entire retinal tree and the embolus was seen to pass into the periphery of the fundus. Within a few days vision was restored.

The effect of quinine on the foetus is worthy of comment. In our case the patient aborted spontaneously; more often the foetus is unharmed and the pregnancy proceeds normally. Professor A. M. Claye, in a personal communication, has suggested that if a large dose of quinine did not produce abortion the foetus would escape serious harm. Nevertheless, it has seemed possible to us, in view of the wide range of sensitivity to this drug, that some unexplained examples of congenital blindness and/or deafness might be due to maternal ingestion of quinine for medicinal or abortifacient reasons.

Finally, it would appear desirable that quinine should be supplied to the public only on a doctor's prescription. Chemists with whom we have discussed this matter have assured us that quinine is rarely purchased nowadays, and only in small quantities, usually for the manufacture of home tonics and wines. Against this view is the fact that our own patient informed us that she had been advised to take quinine by a friend who had herself successfully aborted twice after taking ½ oz. (15.5 g.) of quinine on two separate occasions. Furthermore, a case of quinine poisoning was admitted under the care of one of us (L.G.) at the Royal Halifax Infirmary in December, 1952. This woman took an ounce (31 g.) of quinine sulphate by weight, having purchased it without difficulty at a multiple chemist's shop. She felt ill as soon as she had swallowed the powder, and vomited violently within the first five to ten minutes. She was seen within half an hour by her doctor, who rushed her into the Royal Halifax Infirmary, where the stomach was washed out. She never became completely blind, and her vision recovered fully within three weeks. Whilst writing this paper a further case of attempted abortion by quinine has come to our notice. This woman took an amount of quinine the "size of a sixpence" once weekly for the second two months of her pregnancy. She then gave it up and the foetus developed normally to term. It seems unlikely that our experience is unique. We have wondered whether this dangerous practice is not more common than is realized by the profession or by the pharmacist.

Summary

A case is recorded of complete blindness, of approximately forty hours' duration, due to the ingestion of quinine for abortifacient reasons. Drug therapy was ineffectual, but stellate ganglion block produced an immediate return of central vision and has probably favourably affected the degree of residual loss of peripheral vision. It is suggested that this treatment should

be carried out immediately in all cases of retinal vascular spasm and especially in the treatment of thrombosis of the central retinal vein and embolism of the central retinal artery. The possible dangers to the foetus and the prevalence of the practice are discussed. It is recommended that restriction on the sale of quinine be imposed.

We wish to record our thanks to Mr. R. W. Hendry for his surgical assistance, to Mr. P. M. Wood for the ophthalmic assessments, and to Mr. Norman Emblin, who supervised the gynaecological aspects of the case.

REFERENCES

- Braveman, B. L., *et al.* (1948). *Amer. J. Ophthalm.*, 31, 731.
Cotson, Tullos O. (1951). *Ibid.*, 34, 1289.
Duke-Elder, Sir W. S. (1940). *Textbook of Ophthalmology*, 3, 3033.
King, E. F. (1934-5). *Proc. roy. Soc. Med.*, 28, 354.
Leriche, R. (1952). *British Medical Journal*, 1, 231.
Naffziger, H. C., and Adams, J. E. (1950). *Arch. Surg. (Chicago)*, 61, 286.
Walsh, R. Crosbie (1954). *British Medical Journal*, 2, 684.

RUPTURE OF UTERUS FOLLOWING ACCIDENTAL HAEMORRHAGE

BY

BASIL G. PICKLES, M.B., M.R.C.O.G.
Registrar, King's College Hospital

The incidence of rupture of the uterus is difficult to determine with any accuracy. It is particularly difficult to discover the incidence in Great Britain, as few large-scale reviews are reported, and the standard textbooks refer to series mainly from the United States of America. Brierton (1950) analysed eight large American series which reviewed 368 cases of uterine rupture occurring in 734,932 deliveries, an incidence of 1 in 1,997 cases. Watt (1950), from Canada, reported an incidence of 1 in 1,163 cases out of 17,455 deliveries. Simons (1950), from the Walton Hospital in Liverpool, recorded an incidence of 1 in 2,233 cases out of 33,492 deliveries, whilst the Rotunda Hospital (1952) figures were 1 in 1,333 deliveries. These figures seem to indicate that uterine rupture occurs once in every 1,500 to 2,000 deliveries, as is usually stated. All these figures are for hospital-managed cases. One wonders how truly representative these figures are, for as Titmus (1939) suggested, many cases of rupture are 'probably never diagnosed, being registered as deaths due to haemorrhage or shock.

Analysing 30 maternal deaths, Gordon and Rosenthal (1943) found at necropsy that 11 had a ruptured uterus, the diagnosis not having been made before death. Delfs and Eastman (1945) reviewed 17 cases of uterine rupture occurring in the absence of any uterine scar; in 23.6% the diagnosis was made post mortem. Sheehan (1948) reviewed 147 cases of obstetric shock: rupture of the uterus was found to be the cause in 20 cases.

The possibility of accidental haemorrhage causing rupture of the uterus is not considered by the majority of authors, although Powers and Gerard (1944) mention that in advanced pregnancy uterine rupture may be mistaken for premature separation of the placenta. Fraser (1954) describes two such cases in which a wrong diagnosis of concealed accidental haemorrhage was made, uterine rupture being discovered when a laparotomy was performed after the patients had failed to respond to conservative treatment. The presence of subperitoneal uterine haemorrhage following accidental haemorrhage has been noted many times. Uterine rupture may result when this process progresses a stage