# MEDICAL PRACTICE

## *Hospital Topics*

# Death and blindness due to overdose of quinine

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### Abstract

**During 1953-83 there were 48 admissions to the regional poisoning treatment centre, Edinburgh, for overdose of quinine including 19 since 1978. Six patients were blind and one had ventricular tachycardia. Stellate ganglion block was performed without benefit in seven patients. No patient died, but three deaths from cardiotoxicity occurred in a further 71 patients reported to the Scottish Poisons Information Bureau. Plasma quinine concentration related to time from ingestion was found to be a useful predictor of visual toxicity.**


### Introduction

Quinine poisoning, although uncommon, is increasing and is of particular concern as it may cause long term visual impairment and death. No universally accepted treatment exists for either alleviating visual toxicity or removing large amounts of quinine from the body.

### Patients, methods, and results

The case notes of patients admitted to the regional poisoning treatment centre after an overdose of quinine from 1953 to 1983 were reviewed. During this period there were 48 admissions of 46 patients (13 men and 33 women) aged 15-75, 34 for self poisoning, 12 after attempts to procure abortion, and two after accidental ingestion. Twenty of the patients admitted for self poisoning had also taken alcohol and 15 had taken other drugs, including amitriptyline, benzodiazepines, analgesics, and antibiotics. Two patients had taken aspirin as well as quinine but did not develop symptoms. The average number of admissions during successive five year periods was six (range three to nine) until 1978-82, when there were 14 admissions, and 1983, when there were five.

Plasma quinine concentrations were measured by high performance liquid chromatography using a modified method for quinidine.[1] Quinine concentrations obtained in four patients referred to the Scottish Poisons Information Bureau are also included in this report.

Gastric lavage was performed on 26 occasions and emesis induced on five. Forced acid diuresis was carried out in five cases and charcoal haemoperfusion in one. Stellate ganglion block was performed in seven patients with severe visual impairment.

Of the 48 patients, 36 developed one or more features of quinine poisoning (table I). The mean time from ingestion to onset of minor symptoms was three and a half hours in 26 patients (less than two hours in seven, two to four hours in 10, and four to seven hours in nine). Convulsions did not occur, and there were no deaths. Of 71 further patients reported to the Scottish Poisons Information Bureau during 1963-83, however, three died. Two 2 year old children died, one immediately on arrival at hospital and the other after convulsions, coma, and ventricular tachycardia.[2] The third patient, a woman of 23, developed coma, transient cardiac conduction abnormalities, convulsions, and blindness before dying after cardiac arrest.

#### OCULOTOXICITY

Eight patients developed visual symptoms (table I)—namely, blindness in six (table II), appreciable constriction of the peripheral fields in one, and abnormal colour vision in one. Blindness developed four and a half to 14 hours after ingestion (mean nine and a half hours), although in five patients vision began to deteriorate half to three and a half hours earlier. Five patients had dilated unreactive pupils at some time but fundal appearances were normal at, or when first examined after, the onset of blindness in all except in one (case 4), who had retinal arteriolar constriction at presentation. One patient (case 5) had transient blurring of the disc margins and macular oedema seven hours after blindness developed. One patient (case 2) developed cherry red macular spots after two days when vision was returning, and both he and another patient (case 3) subsequently developed optic atrophy.

Bilateral stellate ganglion block was performed in four blind patients (table III) and unilateral block in a patient who was congenitally blind in one eye (case 5) and another in whom perception of light returned in both eyes

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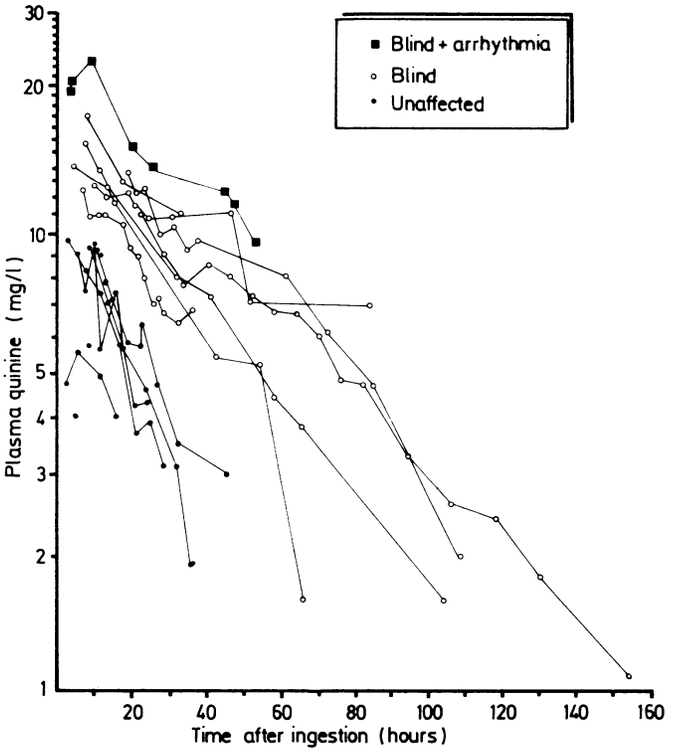
immediately before the first side was injected (case 6). Apart from in this last patient (case 6) the interval between block and first perception of light varied from one hour to four days. Subsequently vision improved slowly (table II), and in those patients who were followed up there was no recovery after two months. Three patients recovered normal vision, but one (case 3) had tunnel vision and had to be registered as blind, although acuity was normal. A seventh patient, with severe constriction of the peripheral fields only, also received bilateral stellate ganglion block without benefit.

In all but one patient (case 5) vision began improving in both eyes simultaneously, and recovery continued in parallel regardless of the interval between the onset of blindness and first block on the two sides. In one patient the procedure was complicated by a tension pneumothorax and bilateral recurrent laryngeal nerve palsy.

TABLE I—*Clinical features of 48 episodes of overdose with quinine in adults*

| Clinical feature | No (%) of episodes |
|---|---|
| Asymptomatic | 8 (17) |
| Unconscious from other drugs | 4 (8) |
| Symptomatic: | 36 (75) |
| Nausea | 26 (54) |
| Vomiting | 19 (40) |
| Tinnitus | 27 (56) |
| Deafness | 24 (50) |
| Vasodilatation | 7 (15) |
| Hyperventilation | 3 (6) |
| Visual symptoms: | 8 (17) |
| Altered colour only | 1 (2) |
| Field constriction only | 1 (2) |
| Blindness | 6 (13) |
| Cardiovascular effects*: | 24 (50) |
| Sinus tachycardia (≥100/min) | 22 (46) |
| Hypotension (systolic blood pressure ≤90 mm Hg) | 5 (10) |
| Pulmonary oedema | 1 (2) |
| Ventricular tachycardia | 1 (2) |

*Excluding patients who took other cardiotoxic drugs.




Plasma quinine concentration related to time after ingestion.

TABLE II—*Plasma quinine concentrations on admission and degree of recovery in six patients who became blind after overdose of quinine*

| Case No | Age | Sex | Plasma quinine on admission* (mg/l) | Time (hours) from ingestion to: Visual symptoms | Blindness | First stellate ganglion block | Perception of light | Duration of blindness | Visual outcome |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 20 | M | 15·7 (7) | 12·5 | 13 | 14·3 | 15·5 | 2·5 h | Normal at three days |
| 2 | 30 | M | 13·5 (18·5) | 11 | 14 | 18 | 33 | 19 h | Optic atrophy and field constriction at eight months |
| 3 | 39 | F | 20·6 (3·3) | Not known | 8 | 10·3 | 4 days | 4 days | Optic atrophy and tunnel vision at one year |
| 4 | 45 | F | 13·0 (10) | 5 | 7 | 8·5 | 20 | 13 h | Normal at one month |
| 5 | 64 | M | | 1 | 4·5 | 12·5 | 13·5 | 9 h | Slight retinal artery constriction at two days |
| 6 | 75 | M | 12·4 (6) | 10 | 11 | 12 | 12 | 1 h | Normal at one day |

* Figures in parentheses indicate hours after ingestion.

TABLE III—*Effect of stellate ganglion block on the patients in table II*

| Case No | No of blocks: Left | Right | Time from first block to perception of light | Signs produced by block | Complications |
|---|---|---|---|---|---|
| 1 | 3 | 3 | 1·2 h | Miosis and ptosis (bilateral) | Hoarse voice |
| 2 | 2 | 2 | 15 h | Miosis (right) and vasodilatation in arms | None |
| 3 | 2 | 2 | 4 days | None | Hoarse voice |
| 4 | 2 | 2 | 11·5 h | Miosis (bilateral) and ptosis (right) | Tension pneumothorax and recurrent laryngeal nerve palsy (bilateral) |
| 5 | 0 | 1 | 1 h | Not recorded | Not recorded |
| 6 | 1 | 0 | 0 | Miosis and ptosis | None |

### CARDIOTOXICITY

Cardiovascular toxicity was usually mild (table I). Two of the three deaths reported to the Scottish Poisons Information Bureau, however, were due to arrhythmias, and ventricular tachycardia occurred in one patient (case 3), who had the highest recorded plasma quinine concentration (23·5 mg/l) (figure). The arrhythmia ended spontaneously eight hours after ingestion. Twenty four hours after ingestion the patient developed gross pulmonary oedema that was unresponsive to diuretics but cleared slowly over the next three days.

Electrocardiograms from 17 other patients all showed some abnormality, including atrial repolarisation changes in four, prolongation of the PR interval in three, and of the QT interval (corrected) (<0·42 s) in 15. The duration of the QRS interval was normal in every case. Minor ST segment depression or slurring occurred in six records, T wave flattening or inversion in six, and prominent U waves in six.

### PLASMA QUININE CONCENTRATIONS

Maximum plasma quinine concentrations ranged from 4·0 to 23·5 mg/l, and visual loss occurred in every patient with concentrations above 10 mg/l. Concentrations related to time from ingestion in nine patients who were blind were higher than in those in eight who were not (figure).

## Discussion

Apart from Elliot's review in 1918[3] no large series of quinine poisoning has been published. Quinine poisonihg is an increasing problem that carries an appreciable risk of temporary blindness and long term constriction of the visual fields. One of our patients had to be registered blind. The mean time of onset of blindness was six hours later than that of the other features of cinchonism. The plasma quinine concentration is therefore a useful predictor of visual toxicity as patients who became blind always had higher concentrations related to time from ingestion than those who did not.

Blindness induced by quinine is widely believed to be due to

retinal arteriolar constriction, but this is contradicted by reports of normal fundal appearances[3-5] and normal arterial calibre on fluorescein angiography[6] in blindness. Arterial changes develop later and progress while acuity improves.[4-6] Moreover, electroretinographic and electro-oculographic studies show early direct damage of photoreceptor cells followed by effects on ganglion cells.[4-7] Stellate ganglion block,[8 9] therefore, has no rational basis, and in our experience and that of others it is ineffective.[10-12] The timing, rate, and degree of visual recovery in our patients were not influenced either by the number of blocks or by the interval between onset of visual symptoms and the first block (tables II and III). Moreover, death[13] and serious complications[13-16] have been reported after the procedure.

Serious cardiotoxicity after overdosage with quinine has rarely been reported[17] and seems less common than with quinidine. Minor changes, however, were present in all electrocardiograms examined; one patient developed ventricular tachycardia, and the three reported deaths were probably related to cardiotoxicity.

The widespread prescribing of quinine for leg cramps is unlikely to be influenced by the fairly small number of patients who die or become blind after overdosage. As stellate ganglion block and measures to enhance elimination of quinine are ineffective[2 11] overdosage should be managed by early gastric emptying and supportive care. Repeated administration of activated charcoal may help to reduce absorption.[18]

Preventive measures are particularly important. Parents and grandparents should be made aware of the risk to small children, and if it must be prescribed quinine should be dispensed only in child resistant containers. Quinine has a bitter taste, and removal of the sugar coating on the tablets might also deter overdosage.

Since this article was accepted for publication the National Poisons Information Service has reported a series of inquiries about quinine poisoning that also emphasises the problems of visual toxicity and the ineffectiveness of stellate ganglion block.[19]

We thank Dr H C Miller for reporting the electrocardiograms, Mrs J Brown for drawing the figure, and Miss J Morris for typing the manuscript.

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*Is flashlight photography harmful to babies?*

The short answer is that no one seems to know. Hamer *et al* measured the visual acuity and rod threshold of nine premature babies who had stayed in a hospital nursery for one month on average[1]: seven of them had undergone phototherapy. Their data did not differ significantly from those obtained on control subjects. Nevertheless, the authors caution against extrapolating these results to others based on different conditions. In particular, their data were obtained long before the completion of retinal development (cf Weale[2]). Hamer *et al* also list conditions that would invite risk—for instance, albinism and large pupils. Past animal experiments are of limited relevance. Howland *et al* have used flash photography for purposes of infant ocular refraction,[3] and no adverse result has been reported so far. Nevertheless, if our information on potential risks associated with a new drug matched what we know on photoflashes and children's eyes permission to use the drug would probably be withheld for the time being.—R A WEALE, professor of visual science, London.

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*A young professional man drinks around 20 pints of lager a week. Recently he has developed a few small spider naevi. His liver function tests are in the upper range of normal. Are the spider naevi of any diagnostic significance?*

In the non-pregnant individual more than four to five spider naevi in the drainage area of the superior vena cava are an important sign of underlying chronic liver disease. Alcoholic liver disease is the commonest form of chronic liver disease to give rise to these lesions, and they may be found not only in alcoholic cirrhosis but also in severe fatty liver. One or two spider naevi may also be found in up to 15% of normal individuals and are therefore not of any diagnostic significance. In the context of a young man drinking approximately 60 g absolute alcohol a day it should be remembered that some individuals are susceptible to developing liver disease at levels of consumption less than the recommended safe upper limit of 80 g absolute alcohol a day, although a normal serum gammaglutamyl transferase activity in this patient would tend to exclude any significant alcohol induced liver damage. Spider naevi developing as a consequence of liver impairment do not necessarily all appear together, and the presence of one or two spider naevi in any individual might therefore be an early stage of development.—ROGER WILLIAMS, consultant physician and director of liver unit, London.

Bean WB. *Vascular spiders and related lesions of the skin*. Oxford: Blackwell, 1959.

*What is the best method of treating discharging ulcers after BCG vaccination? Topical neomycin and hydrocortisone cream is effective but costly.*

Discharging ulcers are rare after BCG vaccination but may occur as part of the immunological reaction. They are said to be commoner if the injection is too deep or if BCG is given inadvertently to someone who is already tuberculin sensitive.[1] Thus infection is not the problem in these cases and cream containing neomycin and hydrocortisone is undesirable for several reasons, quite apart from the price, which is quoted at £6·05 for a 20 g tube of one of the proprietary brands containing neomycin 0·5% and hydrocortisone 2·5%. Neomycin will not alter the immunological reaction. Moreover, the ulcer may persist for months, and repeated application of neomycin may produce contact sensitivity and thus not only fail to do good but cause harm as well. Corticosteroids including to some extent topical hydrocortisone certainly damp down granulomatous allergic responses but other than in exceptional circumstances they are neither necessary nor desirable. Continual application of a cream or ointment to an ulcer tends to keep it soggy so a non-occlusive dry dressing—for instance, a piece of gauze fixed at the edges by sticking plaster—is preferred. In the rare cases when pyogenic infection is superimposed and streptococci or staphylococci are responsible such an infection should be treated in the usual way, ideally with the antibiotic indicated by sensitivity tests, and usually it is best given systemically.—JANET MARKS, senior lecturer, Newcastle upon Tyne.

1 Horwitz O, Meyler J. The safety record of BCG vaccination and untoward reactions observed after vaccination. *Adv Tuberc Res* 1957;**8**:245-71.