

These changes of blood pressure are all-important factors in the operation of intravenous injection of quinine; the more concentrated is the solution, the more likely are they to take place.

Regulation of Rate of Injection.

It may be argued that a concentrated solution may be injected very slowly and so there may be no need of diluting the solution. As pointed out before, to inject 10 gr. dissolved in 200 c.cm. in 20 minutes would require 1 minute for each 10 c.cm. It would, therefore, be necessary to inject the solution still more slowly if a concentrated solution is used, and if it is intended to inject the same quantity of quinine per second. Thus for a solution of 10 gr. in 100 c.cm., one must inject 5 c.cm. in not less than one minute, and the stronger the solution the slower must be the rate of flow and the more difficult to regulate the rate of flow. Concentrated solution of 20 per cent., or 15 gr. in 5 c.cm., as has been recommended by some authorities, would mean that one must inject 5 c.cm. in 30 minutes. It is evident that this is hardly practicable. For the purpose of regulating the flow very accurately, I have devised a specially fine needle with which the flow can be easily regulated at the rate of 10 c.cm. of saline per minute. I have observed that the use of Bayliss's solution in place of normal saline does not tend to diminish the tendency towards fall of blood pressure after injection of concentrated solution of quinine. From what I have stated above, it is evident that the rate of injection should be still slower in the case of children, because if in the adult the limit should be 1/120 gr. of quinine, in the case of children this should be still less. I would suggest that not more than 5 gr. should be injected in patients below 15 years of age in 20 minutes, which is half the rate in the case of an adult.

Two Stages of Fall of Blood Pressure after Inoculation.

The fall of blood pressure after intravenous injection of quinine may take place in two stages: (1) A fall that may take place immediately after injection; and (2) a fall that may come on some minutes after injection has been completed and when the quinine has been well diluted in the circulation.

The former may prove rapidly fatal, the latter may happen whatever may be the dilution of the quinine used. To guard against them I would advise that in all cases of malarial fever in which the blood pressure is low—as is frequently the case with the pernicious type of the disease—intravenous injection

Table showing Results of 5 gr. of Quinine Bihydrochloride dissolved in 100 c.cm. of Normal Saline.

—	Duration of each injection in seconds.	Quantity in c.cm. of fluid injected each time.	Pressure.		
			Systolic.	Diastolic	Pulse.
Before injection	95	65	30
1	40	10	95	65	30
2	30	10	95	67	28
3	40	10	95	70	25
4	45	10	95	68	27
5	35	10	95	70	25
6	25	10	95	68	27
7	35	10	95	70	25
8	35	10	95	65	30
9	32	10	95	72	25
10	40	10	90	65	25
Minutes after completion of injection.			92	65	27
			90	70	20

of quinine should be given guarded with injection of pituitrin or adrenalin. Whatever may be the advantages of a 10 c.cm. syringe, and however simple and quick the procedure may be when it is used, I consider that a concentrated solution of quinine should never be rapidly injected intravenously, and as it may be impracticable to inject such a concentrated solution very slowly, a dilute solution of the strength recommended should always be used.

The accompanying table shows typical effects on systolic, diastolic, and pulse pressures of intravenous injections of dilute solutions of quinine bihydrochloride. It will be observed that the injections were given more or less slowly. In some cases there was still a tendency towards fall of systolic and rise of diastolic pressures. It is to be noted that in this paper "solution of quinine" always means solution of quinine bihydrochloride in normal saline.

Conclusions.

1. In giving intravenous injection of quinine bihydrochloride the solution of the salt should not exceed the strength of 1 in 300; it should be injected at the rate of 10 c.cm. per minute in the case of patients above 15 years of age.
2. The rate should be half the above in the case of patients below 15 years of age.

Clinical Notes:

MEDICAL, SURGICAL, OBSTETRICAL, AND THERAPEUTICAL.

THE SIGNIFICANCE OF

ERYTHROMELALGIA IN CASES OF INTERMITTENT CLAUDICATION OF THE LOWER EXTREMITIES.

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INTERMITTENT claudication of the lower extremities (dysbasia intermittens, angina cruris, &c.) is a syndrome or symptom-complex, occurring on one or both sides, characterised by a feeling of cramp-like pain in the muscles of the calf or instep, which supervenes after a few minutes' walking and obliges the patient to rest, as best he can, before proceeding. It is due to deficient supply of arterial blood to the affected muscles, and this ischæmic condition is nearly always caused by organic obstruction of some kind in the supplying arteries. This syndrome is frequently, but not always, accompanied by the syndrome of erythromelalgia, characterised by pain and turgid redness or cyanosis in the foot, especially when it is allowed to hang or rest in a dependent position. Erythromelalgia, a term originally introduced by Weir Mitchell, is probably not invariably, though in typical cases nearly always, due to organic arterial obstruction.

When the intermittent claudication results from atheromatous or other obstruction high up in the femoral or iliac arteries or in the abdominal aorta, it is not usually accompanied by typical erythromelalgia. But it is nearly always accompanied by typical erythromelalgia in cases of thrombo-angeitis obliterans. My explanation¹ of this is that in the latter disease, which must not be confused with syphilitic arteritis or endarteritis obliterans, the capillaries (not merely the small arteries and veins) ordinarily undergo compensatory enlargement; the obstruction is, in fact, usually in the middle-sized and small arteries, and the capillaries have to take a much greater share in maintaining the collateral circulation than when the obstruction is limited to one or two larger arteries. Erythromelalgia is therefore very significant in cases of intermittent claudication—it signifies that in order to maintain sufficient circulation to prevent the onset of ischæmic gangrene in the foot even the capillary blood-channels have to become dilated. In other words, erythromelalgia is part of the automatic compensatory mechanism in these cases by which the tendency to ischæmic gangrene is resisted. I have known it to be successful when it might have been thought that only amputation could bring relief.

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¹ Quarterly Journal of Medicine, Oxford, 1916, vol. ix, pp. 289-300.