this state of health; people who have come down to the sea-side after a long residence inland frequently develop, after a few days, all the symptoms described. I do not associate these cases with those which are commonly called "lithaemia," or the substitution of uric acid for urea as the final product of disintegration of albuminous substances within the body; in this last condition one finds the more remote symptoms of gout.

What is the exact action of mercury which brings about the happy result? I do not know, nor am I anxious to propose theories. Murchison supposed that mercury possessed a double action, for he says, whether or not the secretion of the bile was increased, more bile was certainly passed when the drug was being taken, and an eliminating action was brought about, so that less of the bile constituents were absorbed from the intestine than usually. Again, he supposed the albumin to be in some way more thoroughly disintegrated. In some such way the brain is "cleared." It is important for us to know empirically the use of a drug which will enable us to give a patient a good night's rest, whilst at the same time we are treating the origin of the trouble and apparently not giving ordinary soporific drugs.

The Danger of putting Old People to Bed.

Probably I shall be running a tilt against someone's opinion when I say that I believe that many old people are sent to bed too early, and are kept too long in bed when they are convalescing. Of course, there are many obvious exceptions which will at once occur to you, and which I need not take up your time in mentioning.

I believe that we should be chary in advising old people to take to their beds when slightly ill. Some few years ago I was attending an old man of 80 with a slight attack of bronchitis, the like of which he had often suffered from before. A consultation was suggested, and the consultant called in advised my patient to go to bed. I remonstrated, but gave way to what I thought then was wiser advice than my own. The patient kept his bed for a week and then died. It may have been a case of *post hoc* and not *propter hoc*; still, my experience has since led me to believe that this man would have had a better chance of recovery if he had remained up during the daytime.

We must remember that the will power of old people is comparatively weak, and that bed to them is comfortable; then, when once in bed, after a few days the heart and muscular system lose tone. The effort to overcome the above is difficult, and sometimes impossible to obtain again. It often requires a good deal of courage to keep these old people from taking to their beds, for the patient often takes kindly to bed himself and the friends think you unkind in advising less rest.

My own belief, then, is that it is wise to keep old people about and with moderate exercise as long as possible.

Final Remarks.

I have finished.

I have often wondered, and at the same time regretted, why men who have been in practice many years do not record their experiences. Men who have been in general practice in the past have done great work. We think of Jenner, etc., and in modern times of Mackenzie.

Some years ago there was much more local record of cases made than there is to-day. In my own experience as Secretary of the East Kent District of the South-Eastern Branch of our Association, for six years we had regularly four meetings a year, with an average of four papers at each session, and with an average of twenty attendances. Things and times are changed. All the papers were written by our own members. Most of us who have been in practice for some years, whether hospital, private, or both, must have a vast experience well worth noting down. I have often said that young men write books, when they have little practice; old men, who know something, have little or no time. Personally I have seen in practice most of the rare diseases in medicine, many of which I have recorded.

We who live in villages and comparatively small towns see diseases often in their true perspective—the beginning, the middle, and the end of them.

HERPES ZOSTER OPHTHALMICUS.

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THE eye has aptly been described as an elegant diminishing mirror of diseases of the body. Indeed, our ophthalmic experience of herpes zoster reflects so diffusely upon epidemiology, neurology, and dermatology that we can but select six arbitrary headings—etiology, pain, efflorescence, keratitis, complications, and treatment.

ETIOLOGY.

"In full fair tide let information flow—

That evil is half cured whose cause we know."

Churchill: *Gotham*, Book 2, 652.

In our infirmary practice the incidence of herpes zoster is approximately 1 in 10,000, but in many clinics it is rarer—for example, Colonel Elliot estimated its relative incidence at Madras at 1 in 25,000.

In twenty private cases the average age at the time of attack was 55. We see the disease in children occasionally, but note that as a rule only elderly patients experience persistent pain, extensive scarring, or severe corneal ulceration. We are indebted to Dr. Henry Head for a letter confirming our inference that ophthalmic zona is more prevalent in early life than ophthalmic statistics denote.

"Herpes zoster in children," he writes, "is almost a negligible disease. Were it not that the mothers are frightened of the rash we should see very few cases in young persons. The elasticity of the ganglia and surrounding parts probably prevents the occurrence of severe forms of pain. Notoriously, herpes zoster wherever it occurs is much more severe in old people than in young. This is particularly the case when the rash lies over the forehead."

Some authors report a preponderance of male patients, and state that the right side is more often affected than the left; in our own series the proportions were equal in both respects. The cases were entirely sporadic. In one instance a man and his wife were affected, but fourteen years intervened between the two attacks. Most of those affected were in good health and were engaged in active mental or physical pursuits prior to some temporary fatigue or minor indisposition, upon which herpes supervened.

In a case which followed carbonic oxide poisoning Sattler first described infiltration, destruction, and degeneration in the Gasserian ganglion. Poulard distinguishes three varieties of trigeminal herpes according to the position of the causative lesion: (1) a neuritic form, affecting the peripheral branches of the ophthalmic division; (2) a rhizomeric form, implicating the Gasserian ganglion; and (3) a metameric form, in which the lesion is in the pontino-medullary nucleus of the fifth nerve. In this nucleus, according to Bing, the frontal region is represented most distally, the temples and eyelids in an intermediate position, and the nose and cheeks highest up. In one or two of our cases anomalous eruptions occurred, for example, on the buccal mucosa, in addition to the eruption of typical rhizomeric distribution.

Netter states that herpetiform eruptions appear in at least 1 per cent. of cases of encephalitis lethargica, and cites a case reported by Medea of Milan, in which encephalitis was accompanied by supra-orbital herpes, followed by paraesthesia of the affected area. Numerous instances of chicken-pox arising in remote farms and isolated villages within twenty-one days of a case of herpes zoster have been recorded.¹⁷ Again, Head and Campbell point out that herpes zoster may justly be described, both on anatomical and pathological grounds, as acute posterior poliomyelitis. Probably the virus of shingles, widespread in an attenuated form, is liable to enhanced virulence, when epidemics arise, and is sometimes inconstant in its affinity for the small bipolar ganglion cells, irritation of which results in the

herpetic eruption. The effects of such irritation are the same whether it be due to a specific virus, or to local inflammatory processes secondary to injury, tuberculosis, or new growth. Patients presenting herpetic eruptions should always, therefore, receive a careful examination.

PAIN.

" . . . and thus would be produced those paroxysms of shooting or flashing pains, which, in accordance with a well known physiological law, are referred to the periphery, although in reality due to a central cause."—Charcot: *Lectures on Diseases of the Nervous System*, Sigerson, 1877, 60.

In mild cases the early neuralgic pain is confined to one side of the head, but in severe and fulminating cases there is intense headache and vomiting. The meningeal branch of the ophthalmic division, which is given off before the nerve reaches the sphenoidal fissure, sends filaments to supply the tentorium; in the rare cases which simulate meningitis in their onset it is possible that the ganglion cells connected with this meningeal branch are implicated. Similarly, according to Chauffard, extension of the disease from the posterior root ganglia to the meninges in spinal zoster would account for the pains down the spine, girdle sensation, exaggerated knee-jerks, and lymphocytosis of the cerebro-spinal fluid which are observed from time to time.

A more typical manifestation is formation; our out-patients complain that the skin feels as though there were something "wick" (that is, alive) under it. Sometimes by rubbing the scalp they produce bald patches, comparable to the frayed sleeve and threadbare coat which proclaim the sufferer from shingles.

In proportion to the age of the patient and extent of the scarring, a type of pain is complained of which has much in common with that which, during the war, frequently complicated partial lesions of the median and internal popliteal nerves—causalgia; a scalding pain is felt in the palm of the hand or sole of the foot, and is increased to a maddening degree by the lightest touch. Causalgia has been attributed to compression of the nervi nervorum. Elderly convalescents from herpes zoster often compare the lancinating pains to the effect of a drop of hot oil, and are careful to avoid cold winds, which are apt to excite a paroxysm. Anaesthesia dolorosa, the duration of which was two years in the severest of our cases, is one of the gravest complications of the disease; Gowers speaks of suicide in despair. Happily cases of such extreme severity are rare.

EFFLORESCENCE.

"Diseased nature oftentimes breaks forth
In strange eruptions."

King Henry IV, Pt. I, Act III, Sc. 1.

The cutaneous manifestations make their appearance in the following order—hyperalgesia, erythema, vesiculation, rupture of the vesicles, cicatrization, and hypaesthesia. Occasionally, according to Poulard, the eruption is haemorrhagic or gangrenous.

The rash usually appears three or four days after the onset of the pain, but this period is not constant; for example, one of our patients suffered from hemicrania for three weeks, and another from intense headache, for the relief of which morphine was required, for only forty-eight hours before the appearance of the rash.

It is sometimes possible, in the prodromal period, to map out the area subsequently affected by the rash by eliciting

a local increase in susceptibility to pain. According to Head and Campbell the eruption is due to intense irritation of ganglion cells which normally produce referred pain in response to afferent visceral impulses. In support of this theory it is urged that those dorsal ganglia are most affected which receive white rami from the sympathetic.

Fuchs records an old clinical observation that there is a striking elevation of the temperature of the skin upon the affected side, which not only is present when the inflammation is recent, but often lasts for a long time afterwards. This increase of temperature is presumably due to antidromic impulses passing from the ganglion, for physiologists

have proved by experiment that stimulation of the peripheral ends of divided sensory roots causes dilatation of the cutaneous vessels.

It has been shown that mustard does not produce its ordinary effect on the skin if it has previously been anaesthetized, nor if the nerves have been divided sufficiently long beforehand to allow them to degenerate.² It would be interesting to ascertain whether the eruption of shingles could be aborted by injection of an anaesthetic such as quinine and urea hydrochloride, the effect of which lasts for some days.

Extensive scarring after trigeminal ganglionitis becomes more common as age advances. The following case illustrates this tendency.

CASE I.

A medical student had been subject to attacks of herpes frontalis every summer since boyhood. More recently attacks had occurred twice a year, generally after examination. When he came under our observation, at the age of 20, he had for the first time reason to complain of residual scarring.

A typical case of herpes zoster ophthalmicus: Confluent ulcers on cornea.

For the most part, our cases have borne out Hutchinson's rule, that when herpes zoster affects the nasal branch of the trigeminal the cornea is particularly liable to suffer. Poulard mentions the fact that the nasal mucosa is often swollen and hyperaemic during the attack, causing unilateral coryza.

A curious superstition is sometimes expressed—that when shingles meets in the middle line the result is inevitably fatal. Bilateral cases of herpes zoster ophthalmicus are

extremely rare. Greenwood of Boston, who reports a case, which showed the multiple scars of the skin along the course of both supra-orbital nerves, so characteristic of herpes, states that one eye was lost from glaucoma and the

other from panophthalmitis secondary to infected herpes corneae. "Il n'est règle qui ne faille."

KERATITIS.

"O loss of sight, of thee I most complain."

Milton: *Samson Agonistes*.

The frequency of corneal complications varies considerably in the experience of different ophthalmic surgeons. Out of 235 cases collected by Willbrand and Saenger the cornea was affected in 83. In rather more than half the cases in our series greyish streaks and opaque areas made their appearance as soon as the rash began to subside. In numerous instances there were vesicles, which ruptured on the surface, leaving superficial ulcers, which remained discrete or became confluent according to the severity of the attack. In one case the opacity was dendriform. Mild iritis accompanied the severer cases.

The current teaching is that herpes zoster corneae is only to be feared inasmuch as it tends to leave a permanent opacity. Thus, according to Mr. Foster Moore, "The ulcers

Diagram showing some of the connexions of the trigeminal nerve mentioned in the text.

never perforate and hypopyon does not arise. . . . recurrences never occur and both sides are never involved." The following case furnishes a notable exception to this generally accepted law.

CASE II.

Male, aged 66. After severe hemicrania for three days an eruption appeared on the right side, which the patient, who had resided in Jamaica, compared to confluent small-pox. The nasal branch was affected. Severe corneal ulceration ensued, with accompanying iritis. The eye was covered with a dressing and treated with atropine and an antiseptic lotion.

At the beginning of the second week, as a result of a consultation with Mr. Teale, paracentesis and syndectomy were performed, without an anaesthetic.

Improvement was only temporary, ulceration continued, and panophthalmitis set in. After consultation with the late Sir Jonathan Hutchinson enucleation was recommended. Enucleation was accomplished without resort to any anaesthetic, no pain being felt.

There was considerable scarring, and the patient complained of fulgurating pains and of a constant sensation—"as though someone had put a plug in his eye and broken it off." Large doses of quinine afforded relief, but on one occasion, after 70 grains in three days, toxic labyrinthitis developed and prevented further exhibition of the drug. The anaesthesia dolorosa lasted for two years.

Anaesthesia of the cornea may persist for months. On rare occasions we have detected a difference between the sensibility of the nasal and temporal halves of the cornea. Clinically there seems little doubt that the neuro-paralytic factor has an important bearing on the course of herpetic ulceration of the cornea, although Turner and Ferrier, by experimental division of the fifth nerve, its root and branches, with protection of the eye from injury, reached the conclusion that keratitis from disease or injury of the trigeminus was the result of irritation rather than paralysis.

COMPLICATIONS.

"It is by no means enough to spend all our pains upon one object."—Horace: *Satires*, Book II, 4.

The following case was complicated by sympathetic irritation.

CASE III.

Male, aged 58. Right herpes zoster ophthalmicus—eruption extending to the tip of the nose. No corneal nor ophthalmoscopic changes detected on repeated examination. Extreme photophobia and lachrymation of the left eye, lasting several months.

Four years later, the patient having suffered an embolism of the right retinal artery, it was ascertained that he was still unable to distinguish between the blunt and sharp ends of a pin on the right side. The left eye was no longer irritable.

The late Sir Jonathan Hutchinson wrote of this patient as follows:

"I have repeatedly known the other eye in cases of herpes to be somewhat irritable, but I do not think I have ever seen a case which approached yours in severity. Have you tried arsenic? It is, I believe, the most efficient remedy for herpetic after-pain. I know a gentleman who suffers from frequently repeated attacks of herpes on the right eyelid, and the attacks are always attended by lachrymation and irritability of the unaffected eye."

Herpetic inflammation of the Gasserian ganglion does not prevent the secretion of tears by the lacrymal gland; the secretory fibres come from the facial trunk, via the great superficial petrosal nerve, sphenopalatine ganglion, and temporo-malar branch of the superior maxillary nerve, which communicates with the lacrymal. Oversecretion by the lacrymal gland of the opposite side furnishes an interesting problem in neurology.

Glaucoma, which complicated three of the twenty cases, occurs in two forms, the treatment of which is essentially different. The first variety is to all appearances idiopathic. There is generally some indication of predisposition to the disease—for example, glaucoma in the other eye previously. It is, in our experience, usually subacute, and tends to occur during convalescence from herpes zoster ophthalmicus, which can only be regarded as an exciting cause. The onset of glaucoma is possibly connected with loss of the normal periods of contraction of the pupil which accompany sleep. An alternative explanation is as follows:

According to Priestley Smith's theory of glaucoma the vitreous is secreted by the pars plana of the ciliary body and the aqueous by the ciliary processes. Senile degeneration affecting the two zones unequally results, it is conjectured, in a relative excess of fluid in the vitreous and displacement of the lens forward. Acceleration of some

such obscure process may be responsible for the somewhat frequent conjunction of herpes zoster ophthalmicus and glaucoma. The following is an illustrative case.

CASE IV.

Woman, aged 56, convalescent from right herpes zoster ophthalmicus. Cornea unaffected. Subacute glaucoma on the same side. (The left eye had been operated on for glaucoma nine years previously.) Right iridectomy. The patient remained under observation for six years, during which time the refraction altered from $1\frac{1}{2}$ dioptries of hypermetropia to 2 dioptries of myopia, with a low degree of inverse astigmatism. When last examined the vision with glasses was R. 6/10, L. 6/60.

Symptomatic hypertension, as certain American authors describe it, may generally be recognized by the presence of punctate deposits on Descemet's membrane or other signs of irido-cyclitis. Secondary glaucoma of this type yields promptly to the use of atropine. The interference with filtration must be attributed to changes in the aqueous.

Herpetic lesions of the choroid, retina,²⁰ and optic nerve⁹ have been reported. Circumscribed nodules on the sclera of reddish colour,¹⁰ the centre of which resembles a limpid vesicle, surrounded by injected vessels, have been observed about a fortnight after the corneal disturbances had declared themselves.¹⁶ Facial palsy and paralysis of the extrinsic and intrinsic muscles of the eye¹ are among the rarer complications of herpes zoster ophthalmicus.

TREATMENT.

Isabel: Alas! what poor ability's in me
To do him good.

Lucio: Assay the power you have.

Measure for Measure, Act I, Sc. 5.

Like other exanthemata, herpes zoster runs its course, albeit at times a painful and protracted one. In elderly subjects, morphine is often indispensable in the early stages; but the danger attending its use in a painful affection which may last for two years is manifest. For one of our patients Gowers recommended the following prescription, which gave relief:

R. Caffeinae citratis	} aa gr. v
Sodii iodidi	
Sodii salicylatis	
Salicini	
Phenazoni	 gr. x

Misce. Fiat pulvis. Mitte in chartulam. Sig.: One paper to be taken every four hours as required.

There is a general prejudice against the use of arsenic, originating in Hutchinson's statement that herpes zoster may actually be caused by arsenic taken medicinally; hence the special interest of his letter quoted above.

Locally, we recommend dusting powders until the vesicles rupture, when cocaine or orthoform ointment is appreciated. In the later stages painting with ichthyol in glycerine, or massage with any simple ointment, is beneficial; hot fomentations should be avoided, as the skin is anaesthetic, and burns are readily produced. Paroleine is a suitable instillation for the conjunctival sac. The intra-ocular tension should be estimated at regular intervals and ocular complications treated as they arise.

Since encountering the case described above which resulted in panophthalmitis, we have several times resorted to suture of the lids. Sir John Tweedy observes that "in very severe cases immediate and permanent relief may be obtained by paring the edges of the lids and suturing them together. Not only does the pain at once abate, but the ulcerative process is checked and repair takes place." We have verified this observation. In elderly patients continuous application of a pad and bandage is apt to produce entropion, retention of secretion, and superficial dermatitis, and the cornea is at the mercy, for so many hours at a time, of any micro-organisms present in the conjunctival sac. Median tarsorrhaphy, on the other hand, provides a natural dressing with adequate drainage. We make a shallow incision along the grey line of the lids, and, introducing three sutures, bring the clefts so formed into apposition. Union is firm on the third day, and the cornea may be inspected by gently separating the outer or inner third of the palpebral margins. The central united portion is divided when corneal sensibility returns—after a period of eleven months in a recent case. The process of healing is

slow and relapses are apt to occur if the lids are separated too soon. Ultimate transparency of the cornea depends largely on complete protection of the delicate corneal surface and freedom from infection.

Median tarsorrhaphy lightly closes the eye as in sleep, compelling it to "hibernate" until its reflex protective mechanism is restored.

BIBLIOGRAPHY.

1. Baranov: *Trans. Oph. Soc. U.K.*, xlii, 167.
2. Bayliss: *Principles of General Physiology*, 1918, 473.
3. Bing, R.: *Compendium of Regional Diagnosis*, 1903, 145.
4. Chaffard, cited by Osler, *Principles and Practice of Medicine*.
5. Elliot, R. H.: *Trans. Oph. Soc. U.K.*, xxxviii, 351.
6. Fuchs: *Textbook of Ophthalmology*, sixth edition, 509, 658, and 659.
7. Greenwood: See Veasey, *Trans. Amer. Oph. Soc.*, xvii, 1919, 297.
8. Head and Campbell: *Brain*, 1900, xxiii, 357, 391, 395.
9. Hutchinson, J.: *Archives of Surgery*, ix, 1898, 136.
10. Mayou: *Trans. Oph. Soc. U.K.*, xxxvii, 1917, 226.
11. Moore, R. Foster: *Medical Ophthalmology*, 1922, 245 and 246.
12. Netter, Arnold: *Abstr. BRITISH MEDICAL JOURNAL, Epitome*, November 18th, 1922, para. 377.
13. Poulard: *Ophthalmologie dans la Pratique Médicale*, 1922, 265.
14. Priestley Smith, cited by Fuchs.
15. Sattler, cited by Head and Campbell.
16. Thompson, G. W.: *Trans. Oph. Soc. U.K.*, 1918, xxxviii, 154.
17. Taylor, Le Feuvre, Evans, and others: *Vide BRITISH MEDICAL JOURNAL*, 1920, i, 283; 1921, i, 382.
18. Turner and Ferrier, cited by Posey and Spiller, *The Eye and Nervous System*, 325.
19. Tweedy, Sir John: *Dictionary of Practical Surgery*, Heath, 1886, 719.
20. Willbrand and Saenger, cited by Weeks, *Diseases of the Eye*, 1911, 287.

THE TREATMENT OF CHRONIC MALARIA.

BY

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QUININE has been long, and still is, recognized as the chief drug for use in malaria, but there is no general agreement as to the best method of administration, and this is my excuse for discussing some results of my experience in its use.

1. Physical Form of Administration.

Sugar-coated pills of quinine are very unsatisfactory, and I have known them, when containing quinine hydrochloride only, cause violent gastric trouble in malaria, and pills so coated are often passed through the bowel undissolved. Even uncoated pills may be so densely compressed, if made of the sparingly soluble sulphate, that a like result may follow; but, on the other hand, if made of the hydrochloride they may dissolve in the act of swallowing so as to give an intensely bitter taste. If taken in 10 to 15 grain doses, whether in this form or as wafers, or in easily soluble capsules, gastric irritation is sometimes set up; this is especially liable to be the case if only a mouthful of water be taken. This result is due to the quinine acting in great concentration on a limited area of the stomach. These troubles can be avoided by administering the quinine in uncoated pill form, using an excipient affording enough cohesion both to prevent it dissolving during the act of swallowing, and to slow down solution in the stomach sufficiently to avoid undue concentration when at least 2 ounces of water are taken with it.

2. Chemical Composition of the Dose.

Unfortunately, for reasons of cheapness, the sulphate has often been the chief salt used, though it has otherwise manifest disadvantages as compared with the hydrochloride, which is soluble 1 in 36 or so of water, is neutral, and in solution less liable to get mouldy. To give quinine sulphate, which is soluble 1 in 800 or so of water, in a mixture to which nearly a minim of dilute sulphuric acid or aromatic sulphuric acid is needed for each grain to secure its solution, is unsatisfactory, especially where large doses, such as 15 grains, are given. The taste is very disagreeable, the acidity is prejudicial to the teeth, and on reaching the stomach both its chemical action and the foreign nature of the mineral acid cause further local and afterwards even systemic trouble. Clinically quinine hydrochloride is better tolerated. Whereas in the case of children pills cannot be used, the sparingly soluble and so less bitter sulphate can be given with syrupy or mucilaginous but non-acid menstrua; the tannate might be better still

3. Route of Administration.

The oral route has in general most advantages, and even where gastric disturbance might be feared adoption of the rules suggested in this paper overcomes it. In severe acute forms the intravenous route would, of course, be the correct one.

Kenneth Mackay¹ found that blood films become negative earlier under oral administration than under either intramuscular or subcutaneous administration, and that four-hourly observations upon the asexual benign tertian cycle appear to show that quinine has an immediate effect upon the malarial parasite—not only upon the young sporulating merozoite but also the intracorporeal stage.

4. Time of Administration.

Marchiafava and Bignami have shown that quinine acts in all phases of the life of the malarial parasite and that therefore it is unnecessary to wait for any specified period. Giemsen and Schaumann found that if quinine were given with the meals traces of it were not found for over two hours, but, given fasting, in twenty to thirty minutes. Kerner demonstrated that, given by the mouth, the hydrochloride is found in traces in fifteen minutes, after the quinine in alkaloidal form in twenty-five to thirty minutes, and that its excretion continued with a meal; whilst Mariani showed that the maximum elimination of quinine in a man's urine occurred between the sixth and twelfth hours if given after food, but between the third and sixth hours if given before it. Castellani and Chambers² say: "With regard to mild quartan and tertian fever, in many cases we give the drug three times a day without regard to the conditions of parasitic life, and this method is apparently not less successful" (than giving the drug four hours before sporulation of the parasite is due).

The following scheme, adapted from MacGilchrist,³ will give some idea of the rapidity of absorption and excretion of quinine after various methods of administering it.

This takes no account of the effects of gastro-intestinal disorders, whether due to malaria or quinine itself or to other causes, in diminishing or in increasing the energy or rapidity of action of a dose, but, so far as my experience goes, by adopting the methods to be subsequently described these are to a great extent negligible.

Hele's experiments⁴ proved that "In active malaria the excretion rate after oral quinine no doubt varies, according to the condition of the alimentary tract, but high fever is not incompatible with rapid absorption and the rapid attainment of the maximum excretion rate, more rapid than after intramuscular therapy." He found no decrease in quinine excretion during continuous administration by the mouth, but that the greater part of the excreted quinine is excreted within twenty-four hours of the last dose, though traces persist for another twenty-four or forty-eight hours. There was no great fall in the quinine excretion till the twelfth hour after a dose by the mouth, till the eighteenth hour after intramuscular injection, and, following the immediate rise, fall, and re-rise in the first half-hour, till the twelfth hour after intravenous injection.

MacGilchrist suggests that a rapid and energetic absorption of quinine is best obtained by giving a salt of it during fasting, then when sporulation is regular to give it two or three hours before the paroxysm, fasting; but where sporulation is irregular to give less soluble forms soon after meals. It is generally agreed that even if a certain amount is absorbed from the stomach, as some assume, the greatest amount is absorbed in the duodenum and practically none (when the drug is given orally) in the large intestine. In practice I prescribe it to be taken an hour before meals and