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Easton, J. A. 1807-1865.
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Publication/Creation

[Glasgow] : [Printed by William Mackenzie], [1858?]

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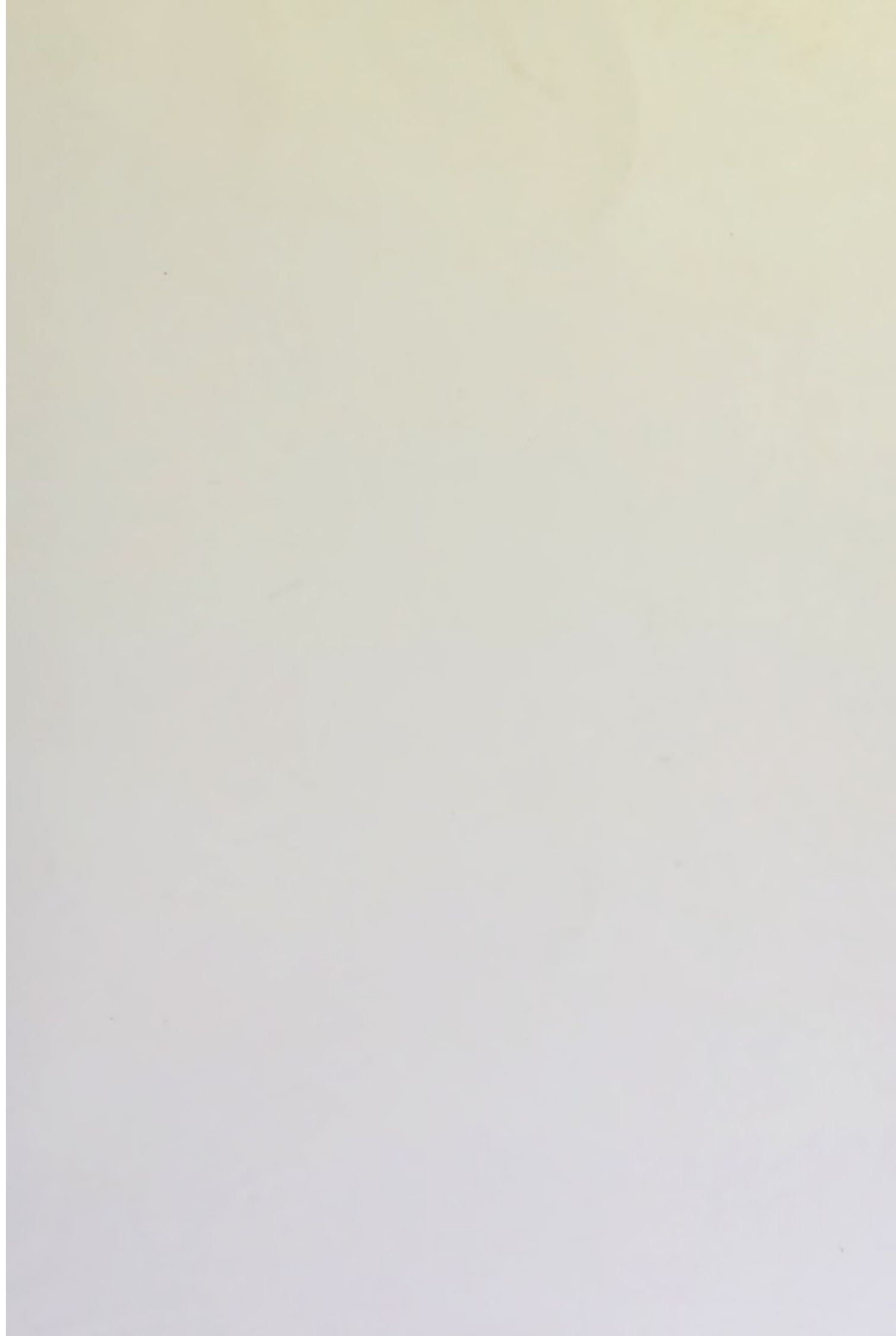
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GENERAL OBSERVATIONS
ON THE
ELIMINATION, CATALYSIS, & COUNTER-ACTION
OF POISONS.

WITH ESPECIAL REFERENCE TO OXALURIA AND AGUE.

(Illustrated Clinically by Cases which occurred in the Glasgow Royal Infirmary.)

BY J. A. EASTON, M.D.,

Professor of Materia Medica in the University of Glasgow, and one of the Lecturers on Clinical Medicine

(From the GLASGOW MEDICAL JOURNAL, Part XXIII., October, 1858.)

UNDER the above title I called attention, in the last number of the Journal, to certain general propositions on the subject of poisons, and endeavoured to show, that while poisons are numerous, and are derived from different sources, and productive of very different effects, they are all, so far as concerns their ultimate disposal, dealt with by nature, and by medical men when they imitate and assist nature, very much in accordance with one general plan. I endeavoured to show that, so soon as a poison is introduced into the blood, nature institutes certain eliminative operations with the view of expelling the noxious ingredient; that these operations are sometimes of themselves sufficient to produce the salutary result; that more frequently, however, they are only partial and comparatively inefficient; and that then, by artificial means, the medical practitioner often succeeds in supplementing the deficiency of nature, by helping her to more successful effort. It was also submitted that the means or processes—both natural and artificial—whereby these results are accomplished, may be described under the general terms, Elimination, Catalysis, and Counter-action. In the former communication, the processes of elimination and catalysis were chiefly referred to, and were illustrated by syphilis and lead poisoning. In this paper, which is to be considered as the continuation and conclusion of the other, I shall principally direct attention to counter-action, and to the

allied operation of prophylaxis ; and in illustration of these processes, I now proceed, without any further preface, to the consideration—

III. OF OXALURIA.—Though oxalate of lime, as is well known, can be introduced into the system from without by the use of rhubarb, sorrel, and some other vegetable substances, yet, with these exceptions, that calcareous salt is always a product generated within, and results either from mal-assimilation of food, from perverted metamorphosis of tissue, or from both these causes combined. When Dr. Golding Bird announced in 1842, in the *Medical Gazette*, that oxalate of lime, which before then had been regarded as a very rare occurrence in urine, was very frequently present in that fluid in certain diseases, and more especially when he affirmed that serious disorders were traceable to a depraved state of the blood, of which the calcareous salt was the manifestation, a new light was supposed to have been thrown upon several morbid conditions, the pathology of which had till that time been obscure. There were some, however, with whom the new doctrine found no favour ; and Dr. Bence Jones, in particular, seconded by Lehmann, did not hesitate to discard it as having no foundation in facts. So far from believing that oxalate of lime in the urine was significant of any peculiar class of diseases, Dr. Jones affirmed that the salt was found indiscriminately, as well in persons in sound health, as in those who were the subjects of widely differing disorders. In the last edition of his work on Urinary Deposits, published in 1853, the lamented Dr. Golding Bird adhered, nevertheless, to the original opinion which he had advanced eleven years before. His views were supported and ably illustrated by the graphic delineations of Dr. James Begbie, in his admirable paper on Stomach and Nervous Disorders, in connection with the Oxalic Diathesis ; and, lastly, as indicative of the opinion on this subject at the present day, we find a writer maintaining, in the July number of the *British and Foreign Medico-Chirurgical Review* for 1858, that, “from every day’s experience, we are led to believe that the views inculcated by Dr. Bird on this subject were correct, and we have a strong feeling that, in the long-run, they will become generally adopted.”

But, without pursuing the controversial part of this topic any farther, I am anxious to elicit the opinion of my professional brethren as to whether or not they have noticed oxalate of lime in large quantities in the urine, in cases of neuralgia generally, and of sciatica in particular. During the last eight months, I have met with nine cases of neuralgia, most of them in hospital practice, in all of which the urine was loaded with that salt ; and though I am aware this cannot be regarded as a new observation, yet I do not think that the circumstance has received that amount of consideration to which possibly it is entitled. On these grounds, and though I may not succeed in establishing a relation

between the deposit in question and any particular pathological condition, I may, perhaps, be allowed to make a few remarks on what appears to be, so far as my experience goes, a tolerably constant and very interesting coincidence. In the first place, looking at neuralgia from a general standpoint—ascertaining the previous habits, manner of life, and present condition of those who are the subjects of it—listening, it may be, to the tale of hereditary transmission, or hearing of the number of victims in the same family circle—noticing the dyspepsia, the occasional hypochondriasis, the unhealthy appearance of the skin, the irritability of temper, the periodicity of the pain, and the variations produced in it by different states of the weather—grouping, I say, all these circumstances together, and drawing from them a general inference, we are warranted, I think, in regarding the neuralgic condition as one of the manifestations of the gouty diathesis. The words gouty diathesis I use advisedly, and in express and avowed contra-distinction to what is both popularly and professionally known as a fit of the gout. This diathesis, I suspect, is of more frequent occurrence than is generally supposed; and the opinion of Sir Benjamin Brodie cannot be too strongly impressed on our minds, that many persons labouring under “what are esteemed local diseases are, in reality, suffering from the influence of gouty poison in the system, though they may have nothing which would commonly pass for gout.” The quaint remark of Captain Grant, quoted by Dr. James Begbie, “that there dies not one of a thousand of the gout, although more die gouty,” is, I believe, in strict accordance with accurate observation, and has been subscribed to, in as many words, by Dr. Gairdner, one of our best writers on gout, who repudiates the notion that we should not consider a man as gouty unless he has suffered under a regular fit of the disease; and states, moreover, his belief, that the gouty diathesis is often very perfectly developed in individuals “who never see”—he does not say who never feel—“its local manifestations,” expressing, at the same time, his conviction, that the strumous is not more frequent than the gouty habit. My belief, then, is strong, that neuralgia is a manifestation of the same poison which is popularly, though erroneously, supposed to develop itself exclusively in the great toe of the aristocratic, the luxurious, and the sensual.

The opinion, in the second place, that neuralgia is a manifestation of the gouty diathesis, gains strength from the observation of the particular tissue in which the pain appears to be situated. The notion, I believe, is very generally entertained, that in neuralgia, the irritating influence, whatever it may be, is exerted not directly on the nerve itself, but on its neurilemma or fibrous investment. Now, while I am aware that the gout poison, or at all events that which is looked upon as its material exponent, may take up its residence—or to express it more in accordance

with the views which I have already offered—may be eliminated and deposited from the blood in any organ or tissue of the body—in the eye, in the ear, the stomach, and even in cartilages and bursæ*—while all this is conceded, I am of opinion, in opposition, I admit, to high authority, that the attacks of gout are more frequently concentrated on the fibrous than on any other tissue of the body, and that, in that particular structure, the poison more especially produces those objective appearances with which every one is familiar. Hence, among the victims of gout, the diffused redness which is so often seen, and the severe pain which is so often felt, in those parts of the body where fibrous tissue prevails, over the dorsum of the foot for example, and in the situation of aponeurotic expansions generally. In making this statement, I by no means wish to homologate the opinion entertained by many, that these particular appearances and sensations, in such localities, are no signs of gout proper, but are the characteristic phenomena of the so-called rheumatic gout, a sort of pathological cross between gout and rheumatism, the deformity of which has been ably exposed by Dr. Garrod.† No one, I apprehend, can read the valuable paper of this accomplished physician on the differential diagnosis between gout and rheumatism, without being convinced that the term rheumatic gout is a misnomer, or rather that it is a name conferred on a nonentity—a title without an estate. Surely these cannot be the same diseases, in the one of which uric acid is always present in the blood in abnormal amount, while in the other it exists only in the usual normal quantity. Yet such has been proved to be the case relatively to gout and rheumatism. They are diseases essentially distinct, incapable of being merged, and therefore not even a hybrid can be expected where union is uncommon, if not impossible. As this is a matter on which it is of great importance that our views should be definite and correct, I make no apology for presenting the following rather long extract from the excellent paper already referred to:—"Can rubeola," asks Dr. Garrod, "become scarlatina, or scarlatina rubeola? Doubtless it is not unfrequently difficult to diagnose certain cases of either of these diseases, at any rate, simply from the present condition of the patient; it is not, however, customary to designate such cases by the compound name of rubeolo-scarlatina, or scarlatino-rubeola; for we feel confident that each of these diseases is produced by a special poison, and has its own special pathology, although the symptoms produced by one may occasionally simulate those of the other. So, also, it may be asked, can rheumatism merge into gout, or *vice versâ*? Has not each of these affections also its own

* On the presence of gouty deposit in the cartilages of joints and in bursæ, see an able and interesting article by Dr. William Budd, in vol. xxxviii. of the *Medico-Chirurgical Transactions* (1855), p. 233.

† *Medico-Chirurgical Transactions*, vol. xxxvii. (1854), p. 181.

special pathology, and is not the name of rheumatic gout, as generally applied, simply a cover for our want of knowledge of the precise affection under which any given patient may be labouring? I would not for a moment be thought to deny the possibility of a gouty patient becoming affected with rheumatism; but I have no hesitation in affirming, as the result of long experience and attention to the subject, that the disease is extremely uncommon, and that the cases ordinarily designated by that name are not those in which such a double disease is present." Returning, however, from this digression, and believing, as I do, that fibrous tissue is the part of the body in which what is considered to be gout proper is perhaps most frequently manifested; and, connecting this circumstance with the favourite locality of neuralgia, I see, in the coincidence, another testimony in favour of the identity of the blood poison, which, in one person, produces severe pain in the fibrous connections of joints; in a second, over the aponeurotic expansions of muscles; and, in a third, along the sheath of some particular nerve.

That neuralgia and gout are mere symptoms of the same blood poison appears probable, in the third place, and more especially, from the chemical history and characteristics of the particular urinary deposit which was found in great abundance in those cases of neuralgia which have furnished the text of these observations. I presume no one will deny that, in the disease to which the term gout is popularly restricted, uric acid exists in abnormal amount in the blood. Now, without affirming either that excess of uric acid, or that deficient elimination of it, which is virtually the same thing, is the cause of gout, we cannot shut our eyes to the fact, that the existence of that acid in abnormal quantity is an occurrence so constant, that it is very properly considered one of the principal pathognomic signs of the malady. If, therefore, we can prove, that oxalic acid is a product of uric acid, if we can prove that the salts of the one acid often replace those of the other, then we cannot regard it as a straining of facts to suppose that there exists absolute identity, in origin and in essence, of two painful affections, called no doubt by different names, but in which the kindred products just specified are found in unusual quantity in the blood and the urine. That oxalic acid is one of the results of the oxidation of uric acid has been demonstrated. Thus, as Dr. Golding Bird remarked long ago, it is well known that a considerable portion of the urate of ammonia existing in guano has been converted spontaneously into oxalate of ammonia during the voyage necessary for the importation of that extensively used manure. Further, Wöhler and Frerichs* found that the introduction of uric acid into the organism was followed by the presence of oxalate of lime in the urine, while more recently,

* *Annalen der Chemie und Pharmacie*, band lxx., pp. 338-42.

Dr. Garrod* has witnessed the production of the same salt from the decomposition of uric acid in blood-serum. The evidence, then, is complete, that the oxalic is merely an emanation from the uric acid ; and therefore, seeing that the latter has been proved to be characteristic of the gouty diathesis, may we not regard the former as equally so, and consider the abnormal conditions, in which we meet with these kindred bodies, as mere symptoms of the same disease, manifestations of the same poison, results of the same morbid action ?

Such were some of the thoughts which passed through my mind when I found the oxalate of lime in great abundance in the urine of so many persons labouring under neuralgia, and observed that in the same patients the calcareous salt was occasionally associated with, or replaced by, uric acid, and the two well known urates. In giving expression to these thoughts I confess to having been very much hampered by the custom so prevalent in medical literature of magnifying symptoms into independent diseases, confounding effects with causes, and perpetuating the error by giving to all of them separate, frequently ill-chosen, and utterly dissimilar names. If this splitting of generic diseases into their more obvious symptoms, and designating each of the latter by a separate epithet were of little consequence, then we might think with Juliet, there is nothing in a name ; but when these different names lead us away from correct pathology and conduct to erroneous practice, then I hold it to be our duty, if we wish to see less nomenclature and more philosophy in medicine, to discountenance, as much as possible, that prevalent habit which leads us to derive our notions of the nature of morbid operations from no other source than the questionable phraseology which professes to describe their more appreciable results. Who could suppose, for example, that neuralgia, podagra, hemicrania, and the other half Greek, half Latin words in the gouty catalogue—sufficiently long to furnish a respectable-looking dictionary of the portable class—were representative only of so many effects of one general cause ? Neuralgia, no doubt, means pain in a nerve ; podagra, that there is a seizure of the foot ; hemicrania refers to half a head ; but it would require a whole head, nay many heads, and very wise ones to boot, to discover that these names referred to three manifestations of the same poison, which nature had thrown out from the blood, in one person, on the sheath of some particular nerve ; in a second, upon the great toe ; and in a third, upon one side of the scalp. Once for all, then, I submit, as a probable circumstance, that what we call lithiasis, oxaluria, gout, neuralgia, *et id genus omne*, are mere symptoms of one general morbid action, to be counter-acted on the same general therapeutic principles. Further, I wish it to be understood, that when referring to excess of uric

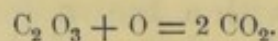
* Medico-Chirurgical Transactions, vol. xxxvii. (1854), pp. 54-5.

acid in the blood, as the constant associate, if not the material exponent—I may not say the direct cause—of gout, I do not mean to convey, that in all cases the excess of that acid is actual. It may be relative, that is, there may be no more than the normal quantity produced; but if there be any defect in the eliminating power of the kidney, then this normal quantity, not being excreted, accumulates in the blood, and hence is found there in excess. At the same time, there can be no doubt that uric acid is frequently in actual excess from over-production, and thus, in the treatment of the various forms of the gouty diathesis, we will do well to remember that the abnormal quantity of acid may be actual, or relative, or both. To this point, however, I shall return in the sequel.

As already stated, the cases which have suggested these observations were nine in number; but so similar were the symptoms in the majority of them, that it were only to weary the reader were I to inflict on him a lengthened repetition of monotonous details, presenting nothing with which he is not familiar, and invested with no interest apart from the urinary deposit to which I have already directed his attention. Suffice it, therefore, to remark, that in one of the cases the circumflex nerve of the shoulder-joint was the seat of pain; in another, the internal cutaneous nerve; in the rest, there was well-marked sciatica. In one of the patients treatment failed to produce the slightest benefit; a second was relieved; a third, while I write, is still under treatment; the remaining six were cured, some of them very rapidly. The treatment consisted chiefly in the administration of 20 drops, three times daily, of the nitro-muriatic acid in an ounce of infusion of calumba; while in those cases in which uric acid and the urates existed in greater quantity, colchicum, acetate of potash, and opium, were more useful. Benefit was frequently obtained from the following combination—*R acet. potass.; vin. sem. colchic. liq. op. sed. a ℥ss.; aq. pur. ℥v.—misce; cuj. mist. sumat. ℥ss. ex aquâ, octavâ quâque horâ.* In those cases in which the tongue was covered with a brown fur and the bowels were confined, two grains of calomel, two of blue pill mass, and five of compound extract of colocynth, followed by a dose of black draught, were often of the greatest service in expediting recovery.

As the *modus medendi* of colchicum and that of acetate of potash relatively to the various manifestations of the gout poison are very well understood, I shall confine my remarks on the treatment which was adopted in these cases, to a consideration of the manner in which the nitro-muriatic acid is supposed to exert a beneficial influence. In all those disordered conditions of the system, in which uric acid, the urates, or the kindred salt, the oxalate of lime, are in abnormal quantity, as in what are called podagra, lithiasis, oxaluria, neuralgia, &c., there must of necessity be a deficiency of oxygen, in consequence of which, the above-

named products of the secondary metamorphic assimilation are arrested in their transitional stages without undergoing that further and final "degradation" which is necessary for their ultimate removal from the organism. Thus, from great deficiency of oxygen uric acid may remain unchanged; or when the supply is greater, but yet not sufficient, oxalic acid only may be formed, and may remain as such, instead of being converted into the last products of oxidation, carbonic acid and urea. These ultimate changes are effected through the instrumentality of oxygen, and thus, in cases of so-called oxaluria, it is to supply the amount of oxygen necessary for "degrading" oxalic down to carbonic acid, that an oxidizing agent like the nitro-muriatic acid is administered. In what way the nitro-muriatic acid supplies oxygen will appear from a consideration of its composition, and of the chemical changes which take place during its preparation. The aqua regia, as this body is generally called, is made, as every one knows, by mixing definite proportions of nitric and muriatic acids. Certain chemical changes take place which it is unnecessary to specify, but for all practical purposes, the result, medically considered, may be affirmed to be the evolution of chlorine and the formation of water. But the chlorine reacts on the water, combines with its hydrogen, sets free the oxygen, and thus earns for itself the title of an oxidizing agent. The chlorine is therefore the real instrument which liberates the oxygen in that nascent state in which its energy is the most intense. A similar reaction is familiar to persons who are engaged in some of the industrial arts, particularly in bleaching, in which process, as is well known, the nascent oxygen, generated under similar circumstances through the agency of chlorine, is in reality the agent by which the bleaching is effected. When, therefore, the so-called nitro-muriatic acid is administered in oxaluria, the oxalic acid is very likely attacked by the now supplemented oxygen, and reduced by it to the condition of carbonic acid, as will probably be better understood by the following equation:—



But it may be asked, How is the lime disposed of, and is not carbonate of lime, equally with the oxalate of lime, an insoluble, and therefore a difficultly eliminable salt? If the above equation, however, correctly represents the chemical changes which ensue, it will be observed, that two equivalents of carbonic acid are formed, under the influence of the supplied oxygen, out of every one equivalent of the "degraded" oxalic acid, and therefore, that the soluble bicarbonate of lime is more likely to be formed than the neutral insoluble carbonate. Besides, even supposing that the latter were the produced salt, it is well known that the carbonates, as a class, are very unstable compounds, and that, as the urine abounds in highly acid salts, the neutral calcareous car-

bonate, if present, would very soon be broken up and disappear under their influence.

It may be objected to these views, that they are theoretical rather than practical, savouring too much of the chemical materialism which many regret is prevailing so extensively in the medical literature of the day, and I am quite prepared, consequently, for a large amount of ridicule, and of sneering at the absurdity of resorting to chemical equations and blackboards for the elucidation of pathological and therapeutical changes. It is at all times, however, more easy to ridicule than to refute; and though our attempts to arrive at truth may be often unsuccessful, it is better, I maintain, to make these attempts than to plod on in miserable routine, without being able to assign any reason for the course we are pursuing. Better, surely, to give some reason, even though it be a wrong reason, than to give no reason at all! At the same time I need scarcely add, that we should not doggedly cling to a theory which has been proved to be wrong, but should instantly abandon it in quest of a better. An objection of some weight, however, may be urged against the pathological views which have now been advanced, on the ground, that, assuming them to be correct, they refer merely to an effect, and not to a cause. The oxalate of lime, it may be said, is not the disease, it is merely a sequence of some antecedent morbid condition, and the rational practice would be to alter that condition, and then there would be no such sequence at all. Now, I am not sure that we should greatly err if we affirmed, that, in those cases of oxaluria of which neuralgia is the prominent symptom, the oxalate of lime is in reality the *immediate* cause of the pain which is felt. It will not be considered improbable that the calcareous salt may be deposited in the neurilemma, and if it be, pain of necessity will be produced in the nerve with which the foreign body is in contact. We know that the presence of urate of soda in the several structures of joints, including even their cartilages and bursæ, is the chief cause of the sufferings of the victim of gout, and there is no reason why a similar result should not follow the deposition and imperfect elimination of the oxalate of lime. At the same time I readily admit, that he who is imbued with that spirit of philosophical inquiry which ought to animate every member of our profession, will not rest satisfied with the mere knowledge that oxalate of lime is present, but will try to find out why it is present, whence it has come, and what is the precise nature, and what the signs, of that antecedent constitutional error which has generated the abnormal product. In the course of these remarks I have more than once alluded to the fact of uric acid being in excess in the blood of those who are suffering from gout, and I have also spoken of that excess as being the result of actual over-production, of deficient renal elimination, or

of both causes combined. I would not have the reader to suppose, however, that I regard uric acid and gout as synonymous, interchangeable terms which are descriptive of some general morbid cause. On the contrary, I regard these phenomena merely as effects, but I submit that the very constancy of their association throws some light on the kind of previous action which manifests itself in their simultaneous production. In support of this opinion we have only to look at the habits and manner of living of those who are the subjects of gout in its most familiar and unequivocal aspects, and at the class of persons on whom it inflicts its unwelcome visitations. As a general rule, does it not select for its victims those who indulge in highly nitrogenous articles of diet, and in whom, consequently, actual over-production of uric acid, irrespective altogether of deficient elimination, must follow as a matter of course? The well-known experiments made by Lehmann on himself, with the view of determining the amount of uric acid excreted under the use of different kinds of diet, are conclusive as to the power which we have either to create that acid in excess, or to diminish it, as we think proper, by the mere quality and quantity of our food. By undeviating observance, then, of the peptic code, enjoining strict conformity with its salubrious regulations, aided by pure air, regular habits, moderate indulgence in sleep, and healthful exercise of mind and of body, we may do much to counter-act even a hereditary tendency to that condition of the system, which, if not controlled by such hygienic checks, may generate uric acid in excess, and characteristic bodily suffering as its concomitant. And in the cases of those actually suffering from the disease, what adjuncts to medical treatment are so beneficial, as the dietetic restrictions and the general hygienic counter-action to which I have just referred? Further, the gouty diathesis may display itself in other forms and among a different class of patients. If it has been proved that oxalic acid is a product of the oxidation of uric acid, and if it has been rendered probable—and, *a fortiori*, if more extended observation shall make it certain—that the former acid is the associate, or material exponent, of that manifestation of the gout poison known as neuralgia, then we can easily understand how the working and middle classes, taking more exercise, and necessarily consuming more oxygen than the idle and the luxurious, may exhibit the kindred products, oxalic acid and neuralgia, as *their* manifestation of the gout poison, rather than uric acid and pain in the joints. If these views be correct, then we may have some conception of the circumstances which regulate the several evolutions of the one, internally generated, poison, and may learn how the state of the system which produces it may be counter-acted, or rather prevented, with little assistance from medicine, and by depending chiefly on dietetical and hygienic means.

It is time, however, that I should pass on to the last illustration of the theme which I have selected, and therefore I shall now make a few observations

IV.—ON AGUE.—The cold, hot, and sweating stages of intermittent fever, the periodical recurrence of these stages at regular intervals, and the comparative remission from suffering which exists till the dreaded paroxysm returns, are phenomena so constant and so characteristic, that they must have forced themselves on the attention even of the unthinking multitude, from the first moment that ague attacked the human race. Nor is there any malady regarding the origin and the treatment of which there is so little difference of opinion among medical men. All agree in ascribing the disease to malarious influence; all are convinced that the periodic paroxysm is but the manifestation of a poison conveyed from without into the blood—*ima per ossa currens*—and no sooner is the word ague pronounced than arsenic, cinchona, or some other febrifuge vegetable bitter immediately presents itself to the mind. But in this zymotic malady, as in others of a similar origin, nature takes the first step in the work of recovery; here also, as in other instances, there is the usual attempt at the expulsion of the disturbing ingredient, and the unbroken though oft-exhibited concatenation, with its three familiar links, displays the regularity, as well as the extent, of the natural eliminatory effort. That effort, however, as in many similar conditions, is ineffectual, or, at all events, it secures no immunity against the future working of the remanent and still uncontrolled poison. True, indeed, at the end of each paroxysm, when the worn-out victim of ague is drenched with perspiration, he can console himself with the assurance that his exhausted frame shall enjoy comparative repose during the three days, or the two, or certainly during the one day which is to follow, and witnessing these intervals of remission, we can scarcely resist the conclusion, that a portion at least of the noxious ingredient has been removed which had caused so much reactionary tumult in the system. But the ague poison, like some other poisons, is evidently of a cumulative character, and is not to be disposed of by the recurrence of those sanatory paroxysms which nature institutes with such tantalizing regularity. The imponderable agent cannot thus be exterminated, the ague diathesis must be met by artificial counter-action, and hence the aid of medicine is required to supplement the deficiency of nature, and to triumph over the obstinacy of disease.

As already mentioned, the catalogue of remedies employed against ague is a very short one, comprising only arsenic and a few vegetable bitters, such as cinchona, bebeerine, augustura, salicine, &c., of all of which remedies the disulphate of quinia, or quina, as it now more shortly called, is by far the most generally administered. Though no one will gainsay the statement that

this salt is a most valuable medicine in ague, it is impossible, I fear, in the present state of our knowledge, to offer an unchallengeable explanation of the manner in which it produces its beneficial effects. In these circumstances, therefore, the most prudent course possibly, and the one least likely to fasten on us the charge of presumption, will be to examine the most prominent opinions which have been presented on this subject, to show how the medicine evidently does not operate, and thus we may clear away some obstructions, and narrow the ground for at least more plausible speculation regarding the true mode of action. First, quina, though foremost among the tonics, does not eradicate the ague poison from the system by the induction of those results, of an exclusively tonic character, which are properly ascribed to that valuable class of medicinal agents. Various definitions have been given of tonics in accordance with the views entertained of their *modus operandi*. To repeat these definitions would be irksome, and therefore, without in the slightest degree attempting to disparage the distinguished men by whom they have been offered, I may be allowed to submit the following definition of tonics, which I have long taught, as being in my opinion the most comprehensive, and the best supported by facts. A tonic, then, I would define to be a medicine which, commencing its action on the stomach itself, very likely by stimulating its nerves and muscular fibres, improves the appetite, strengthens digestion, and favours assimilation, helps, consequently, to make good blood, which in turn furnishes good tissues—a medicine which adds vigour to the circulation, which promotes secretion when defective or represses it when morbidly increased, which braces the nerves, imparts tone to the muscular system, and renovates the power and functions of the whole animal economy, over every department of which it exercises a pervading and permanent influence. Further, a tonic, unlike a stimulant, produces its effects only on the diseased, the infirm, and the convalescent. It does not make a strong man more strong, though it makes a weak man more robust. Now, many vegetable bitters have these properties in perfection, and yet exercise little, if any, power over those diseases which are characterized by periodical exacerbations; and as has been well remarked by Dr. Headland, it is worthy of notice that this observation applies more especially to some of the more common bitters, such as quassia, calumba, and gentian, which owe their efficacy not to alkaloids, but to neutral principles. But the ague poison is not overcome through the induction of any of the effects described above, as being characteristic of tonics, and which description, I venture to state, will be found to accord with faithful observation. Nay more, it has been shown by Dr. Bryson, to whose valuable observations and suggestions I shall advert more fully in the sequel, that quina, administered to sailors in perfect health, while cruising in certain latitudes in which ague was pre-

valent, has acted as a prophylactic to such persons, and has enabled them to pass unscathed along those pestilential shores, whence noxious exhalations had often proved disastrous to others, who had not subjected themselves to similar precautionary discipline. Few will maintain that an effect like this is produced by a mere tonic, which, as I have already stated, exercises no power for good or for evil over persons who are in the normal condition; and therefore, while we must admit that quina is an excellent tonic, considered purely as such, we must believe that it is something more than a tonic, and that when it cures ague, it does not conduct its febrifuge operations in accordance with, what I may be allowed to call, tonic principles.

In the second place, a careful and unbiassed observation of the effects of quina in the treatment of ague will convince us, that the salt does not operate by inducing catalysis. Catalytic agents, administered as remedies, being, as I remarked in my former paper, foreign to the economy, cannot be assimilated, are therefore poisonous, and must be expelled from the system. Hence they are found in most of the excretions, particularly in the urine and saliva, in some instances along with the noxious substance against which they had exerted their power. Now it would be unfair to deny that, in one respect, quina sometimes conducts itself after the manner of catalytics, inasmuch as in some exceptional cases, and only when a large dose of the salt has been taken, headache, flushing of the face, and other symptoms of cerebral disturbance occasionally ensue. No doubt in this aspect the medicine may be said to exhibit something like toxic properties; but there is this essential difference between it and the recognized catalytics, that whereas the injurious effects of the latter are constant, those of quina are comparatively rare, being seldom met with except when the medicine has been administered in a very large dose. Moreover, there is this other characteristic distinction between quina and arsenic, and the catalytics generally, that while the latter are utterly inassimilable, and must consequently be excreted, the alkaloidal salt is apparently in great part retained and incorporated, or is converted into some other material, for chemical analysis has either failed altogether to detect quina in the excretions, or in quantity so small as to be out of all proportion to the amount which had been administered. This statement, however, it is but fair to notice, receives a seeming contradiction from the observations of M. Briquet at the Académie de Médecine, as these are reported by the "Paris correspondent" of the *Medical Times and Gazette*, in the number of that periodical for 2nd August, 1856. According to the "correspondent," M. Briquet "has found that quinine passes very quickly into the urine. In half an hour after it has been ingested it is found in the urine, but the complete elimination of a dose requires many days. Urine seems to be the only secretion with which quinine is eliminated." I have not had an opportunity of seeing the original paper, nor have I

observed any other reference to it, either in corroboration or disproof of the statement now advanced. So far as I know, therefore, the observation of M. Briquet has not been confirmed by others; but even supposing it to be correct, the results do not, in my opinion, imply catalytic action on the part of quina in the cure of ague, but rather the reverse. It is well known, as I shall show in the sequel, even from my own very limited experience, that quina, when it does cure ague, generally counter-acts it very rapidly, a fact which is quite inconsistent with the statement that "a dose" requires "many days" for its elimination. It will, of course, require many weeks to eliminate *several* doses; but long before such a period, nay, even in a single day and from a single dose of quina, ague has frequently vanished. The statement of M. Briquet, however, demands, and I have no doubt will receive, attention. Meanwhile, and in support of the non-catalytic theory, I submit the following extract from the valuable work of Dr. Headland on the action of medicines.—"Quina is not necessarily excreted from the blood. That is, it appears that when given in small or medicinal doses, it is not excreted at all; but when given in an excessive or overdose, quina, like other restorative medicines, will make its appearance in the urine. Wöhler and Freichs could not at first discover quinine in the urine, but they obtained proof of its presence there after administering a large dose. Dr. W. Herapath, of Bristol, made a very careful analysis of the urine of a patient suffering from tetanus, to whom forty grains of the officinal disulphate were administered in the twenty-four hours. In half a pint he discovered an amount of quina equivalent to 1.884 grains of the above salt; and supposing two pints of this secretion to be voided per diem, this indicates 7.536 grains as excreted from the system, out of forty grains ingested."

For the reason that they are contradictory, and based on too limited observation, I pass over the respective opinions advanced during last year by Drs. Ranke and Stuart, and proceed to remark, thirdly, that the bold hypothesis of Dr. Headland, that intermittent fever is cured by quina, in consequence of the salt replacing taurine, which is said to be deficient in ague, must be regarded as still more untenable than the theories which have already been presented. With unusual speculative boldness, and startling originality of conception, Dr. Headland hazards the speculation—and devotes several pages to its exposition—that as in ague there exists disordered function of the liver, the morbid manifestations of the ague-poison may be owing to a deficiency of the biliary principle, known as taurine, and which Liebig maintains is re-absorbed into the blood from the bowels; and that as quina bears a considerable resemblance in its atomic composition to taurine, so it is conceivable, that the beneficial effects of the salt may be owing to its furnishing to the blood an analogue compensatory of the absent or deficient biliary ingredient. Quina,

therefore, according to this view, cures ague neither as a tonic nor as a catalytic, but as a restorative; and this is done by the introduction into the blood of an agent which has a fancied similarity of atomic composition with a supposed biliary constituent, assumed for the time being to be absent or deficient in the victim of ague. It certainly is not to be expected that the correctness of a theory should be susceptible of demonstration, for then it would cease to be theory by having passed into the region of fact; but on the other hand, we cannot be blamed for rejecting a speculation, however ingeniously devised or skilfully exhibited, which is demonstrably based upon error. Unfortunately, then, for this theory, in healthy bile there is no such principle as taurine; and, as regards atomic composition, to use the words of a facetious therapist whom I shall presently name, "taurine is no more like quinine than chalk is like cheese." On the authority of Lehmann, as quoted by Carpenter,* there exists in healthy bile, not taurine, but the conjugated acid, called taurocholic, not in the free state, however, but in the form of alkaline taurocholates; and when bile undergoes decomposition, or is subjected to certain chemical operations, which it is unnecessary to specialize, taurine is then set free, being a product of the chemist, and not an educt from the normal secretion. And further, according to the researches of Redtenbacher, as recorded by the author just named, taurine always contains 25.6 per cent. of sulphur; of which elementary body, however, quina contains not even an infinitesimal trace. On these grounds the taurine theory cannot be accepted even as a theory, and in dismissing it from consideration, I shall only remark that it has supplied an excellent subject for the infinite jest and elegant satire of Dr. Douglas Maclagan.

In making these strictures on the speculations hazarded and expounded, though certainly not insisted on, by Dr. Headland, I beg to assure my readers that I have discharged this part of the duty which I owe to them with the greatest pain and reluctance, for in common, I believe, with every teacher of the *Materia Medica*, I feel deeply indebted to that gentleman for by far the ablest, the most ingenious, and original work on the action of medicines which has appeared in modern times. And it is just because of the great talent, originality, and industry which are displayed in that work, that my regret is increased that a treatise, otherwise so excellent and complete, should still continue to be disfigured in a second edition by a manifest blemish, which had already been pointed out in no unfriendly spirit by the eminent therapist whose name has been mentioned above. Yet, though in the present instance we must regret that *bonus dormitat Homerus*, it is only by a soberly-conducted and pains-taking scrutiny of the processes of nature, and by availing ourselves of all the improved modes of inquiry of this inquiring age, that we can ever hope to

* Carpenter's Physiology, p. 69.

arrive at rational notions regarding the *modus operandi* of medicines. Let us not, therefore, abandon these unsolved problems in despair; and in reference more particularly to the subject which we are now considering, let the very obscurity which hangs around it only stimulate to greater zeal in future investigations. But let our zeal be according to knowledge; and though at present we may not be able to arrive at a satisfactory solution of the difficulty, we can at least disentangle our minds from preconceived opinions, and thus, under the persuasion that quina cures ague neither as a tonic, nor as a catalytic, nor as a restorative, we may narrow the field for future and more successful inquiry.

In the meantime, it being admitted that the phenomena of ague are the manifestations of a peculiar poison in the blood, and it being undeniable that quina cures the disease, it appears to be a fair inference, that the medicine, in its relation to the poison, exhibits the behaviour, and in some respects answers the description, and deserves the name of, an antidote. It does not militate against this assumption, that we cannot detect in the excretions any new compound which has been formed between the bane and the counter-acting agent. The poison itself is subtle and intangible; its pernicious operations are conducted in a laboratory which is not open to human inspection; and therefore, while in the nature of things we may not have direct proof of antidotal influence, such as is afforded in many instances where other poisons are rendered inert, we have the evidence of undoubted salutary change, and of unquestionable analogy in its favour.

In our present ignorance, however, of the chemical composition and physical properties of malarious poisons, speculation is profitless, and therefore, without any further theorizing, I shall illustrate the beneficial effects of quina in the treatment of ague by the following cases:—

John Jones, aged 30, seaman, was admitted into the Glasgow Royal Infirmary on the 15th December, 1857. Patient has had tertian ague for four months. Was attacked with it first while in Carthage, New Granada. Paroxysm comes on during the night, and recurs at intervals of two or three days. Of late has had headache, is hot and feverish, and there is some dulness over the left hypochondrium, though no tumour is perceptible. *R disulphat. quin. gr. xv.; acid sulph. aromat. gtts. xv.; aq. ℥ii—misce; fiat haustus horâ somni sumendus.* The following mixture was also prescribed: *R disulph. quin. gr. xxxvi.; acid sulph. aromat. q. s. pro solut. aq. ℥ vi.—misce; cuj. mist.umat. ℥ss ex aquâ ter in die.* After taking the first dose there was no return of the paroxysm, nor did any more occur, though the patient remained in the hospital till the 9th January, 1858, on which day, being anxious to rejoin his ship, he was dismissed, I can scarcely say cured, for that event had taken place nearly a month before, under the influence, apparently, of the one large dose of quina.

John Gray, aged 23, seaman, was admitted into the Glasgow

Royal Infirmary on the 14th December, 1857. Patient left Alexandria, in the state of Virginia, North America, at the beginning of last month. Has had quotidian ague for two months, and his strength is much reduced. Paroxysm, which at first came on at midnight, now occurs at uncertain hours, though it returns more frequently about six p.m. than at any other period of the twenty-four hours. It is apparently induced by exposure to cold or moisture. *Horâ quinta, p.m., capiat æger disulph. quin. gr. xv.; in acid. sulph. arom. gtt. xv., et aq. ʒii.* This draught was given every evening, and three times during the day he took five grains of quina in addition. The paroxysm returned as before for two consecutive evenings, but on the fourth day after admission it was reported in the journal that "the paroxysm came on last night several hours later than usual." On the 19th December, the fifth day from admission, the patient was ordered fifteen grains of quina morning and evening, the five-grain doses being continued as before. From that day there was no return of the paroxysms, and on the 9th January, 1858, being anxious to go out with his brother in profession as well as in suffering, he was dismissed from the hospital perfectly well.

To these two cases I might add other three, treated in a similar way, and successfully, during my former incumbency in the hospital, but the value of quina in the treatment of ague is so thoroughly appreciated, that I think it unnecessary to furnish additional illustrations. But while the benefit of quina in the treatment of ague actually existing is so well known and availed of as to render further comment on that subject superfluous, it may not be unprofitable, while it will certainly be illustrative of one of the propositions set forth in this paper, to direct attention to the prophylactic virtues of the medicine, and to the suggestions regarding the manner of using it, which have been made by our former townsman Dr. Alexander Bryson, an old alumnus and graduate of this university, and now one of the deputy-inspectors of Her Majesty's navy. Convinced by long experience and close observation of ague, that the poison may develop itself a considerable time after malarious latitudes have been departed from, Dr. Bryson suggested that quina should be administered as a prophylactic, "and that its use should be continued, not only while the men were exposed in unhealthy localities, but *for at least fourteen days after they returned on board*, in order that the antagonistic influence of the medicine might be kept up until the incubative period of the disease had expired." * In accordance with these suggestions, a strong spirituous solution of amorphous quinine was mixed with several pipes of wine, in the proportion of four grains of the salt to an ounce of wine, and of this mixture an ounce was administered and repeated, and continued according to circumstances. Abundant proof of the success of this treatment is furnished in the reports of

* Report on the African Station, p. 219.

the several medical officers on the African station, under whose superintendence the quinine was administered as a prophylactic agent. From these reports I make one or two extracts :—

“The gig from Her Majesty’s ship *Teazer* was detached in the Boom-kittam ; quinine wine, in the usual dose, was given night and morning, and continued for fourteen days after its return. A boy (William Roberts), from dislike to the quinine, took at most but three doses. He was the only one of the boat’s crew that suffered from fever, which occurred ten days after leaving the river. While coaling at Sierra Leone an extra allowance of quinine was given to each man ; Mr. —, however, placed no faith in its preventive influence, and would not take it, and he alone suffered an attack of fever, which proved fatal.”

One extract more :—

“Thirty-six men belonging to the *Water Witch* were employed at the attack on Lagos ; they were in the river four or five days, and, with the exception of three, all took quinine wine while there, and for fourteen days after they left it. Of the whole number, five only were attacked with fever, namely, the three men who did not take the wine, and other two, who most imprudently exposed themselves to the sun, and bathed while much heated by violent exercise.”

In strong contrast with these results, and conclusive, in my opinion, as to the prophylactic virtues of quina against ague poison, it is stated in one of the reports that a whole boat’s crew was seized with fever, no wine having been administered, in consequence of the whole stock having been lost while crossing the bar of one of the rivers on the east coast of Africa. The importance of Dr. Bryson’s discovery can scarcely be over-estimated, not only in its application to soldiers, sailors, and others engaged in the public service in malarious localities at a distance, but also to persons nearer home who require to be in inconvenient proximity with what are popularly known as the fenny districts. I think further, and in conclusion, that a consideration of the peculiar circumstances now detailed under which quina was administered, as well as the success which attended its administration, will convince us that the medicine, in some inexplicable manner, produces such an alteration in the system as enables it to bid defiance to the contact of that malarious poison which for centuries has displayed its distinctiveness and its power in the phenomena of ague. It will not be denied that the mysterious entity, whose unseen exhalations send forth desolation and death, has been disarmed of its potency by a palpable counteracting agent ; and thus we are justified in maintaining the opinion already expressed, that counter-action sometimes takes place without catalysis, though catalysis always implies counter-action.

