#### Gout and goutiness and their treatment.

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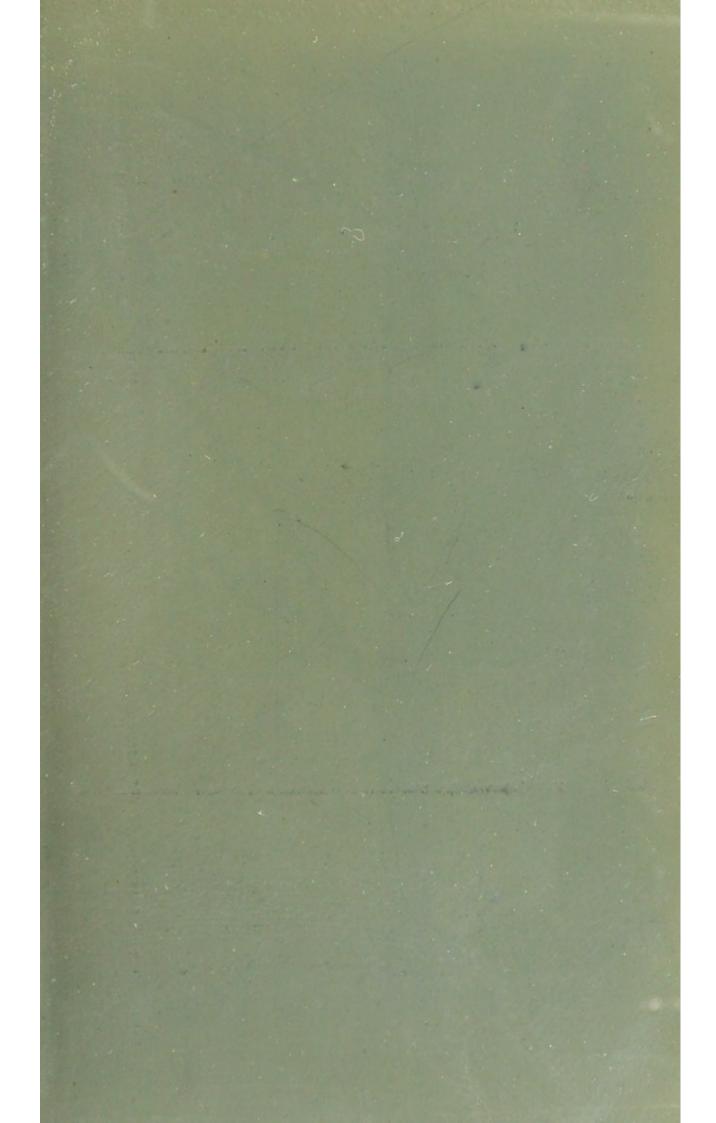
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GOUT AND GOUTINESS;

AND THEIR TREATMENT.

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- Symptoms and Physical Signs: a Formulary for Clinical Note-taking, with examples. Small 8vo. London: Baillière, Tindall and Cox.
- How to Feel the Pulse, and what to Feel in it.
  With 12 illustrations. Post 8vo. London: Baillière, Tindall and
  Cox; New York: William Wood and Co.
- Cardiac Outlines for Clinical Clerks and Practitioners. Post 8vo. London: Baillière, Tindall and Cox; New York: G. P. Putnam's Sons.
- Heart Studies, chiefly Clinical. I. The Pulse Sensations: a Study in Tactile Sphygmology. London: Baillière, Tindall and Cox; New York: William Wood and Co.

# GOUT AND GOUTINESS:

AND THEIR TREATMENT.

BY

## WILLIAM EWART,

M.D. CANTAB., F.R.C.P. LOND., M.R.C.S. ENG.,

PHYSICIAN TO ST. GEORGE'S HOSPITAL, AND TO THE BELGRAVE HOSPITAL FOR CHILDREN;

EXAMINER IN MEDICINE AT THE CONJOINT BOARD;

FORMERLY ASSISTANT-PHYSICIAN AND PATHOLOGIST TO THE BROMPTON

HOSPITAL FOR CONSUMPTION.



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## WILLIAM OSLER, M.D., F.R.C.P.,

Professor of Medicine in the Johns Hopkins University, and Physician-in-Chief to the Johns Hopkins Hospital, Baltimore,

This Work is Dedicated,

IN ADMIRATION OF HIS GREAT SERVICES TO SCIENCE
AND TO CLINICAL MEDICINE,

BY HIS FRIEND THE AUTHOR.



#### PREFACE.

The renewed attention devoted during the last few years to the study of gout, whilst bringing us nearer to the desired solution, has, for a time, rather complicated the problem. The varied and often conflicting results of recent pathological research have had a disturbing effect upon our therapeutics, and further confusion has been occasioned by the perplexing number of new remedies claiming to possess chemical control over the affection. A striking illustration of the prevailing uncertainty is furnished by the strange contrast between the opposite methods which are now put forward as the rational treatment for gout.

This period of transition, although ill suited for any constructive effort in the direction of pathology, seems to be an opportune season for a reconsideration of our principles of treatment, and this is the task to which the present work addresses itself. Since, however, a critical study of the therapeutical questions inevitably opens up others connected with pathology, the best introduction to it will be to review the subject of gout in its entirety rather than in a fragmentary fashion.

In carrying out this preliminary inquiry, a clear and systematic account of the views which have been entertained, and of those personal to the writer, has been aimed at. All future students of gout must be indebted to Sir A. Garrod's great work, to Sir W. Roberts' brilliant researches, and to the exhaustive treatise by Sir Dyce Duckworth. A prominent place belongs in these pages to the facts and to the opinions of these authorities. They also contain references to the important works of Ebstein, of Lecorché, and of Rendu. Recent pathological investigations, of which Dr. Levison's book supplies an able digest, have been noticed; and special attention has been devoted to the latest and not least original views published in this country on the clinical aspects of the affection.

The treatment of gout, which is the main subject for study, has been dealt with on the same lines of systematic and, so far as possible, practical exposition. The distinction between gout and goutiness, familiar to all observers, has received special recognition, as one which is essential to clearness in all discussions on the pathology and treatment of the affection.

The bulk of this volume, not the least of its faults, is partly explained by the recent expansion of the literature of gout, and by the desire—imperfectly fulfilled—to deal with it adequately.

The author is under obligation to Dr. Arthur Herbert Hoffman, of Old Burlington Street, for important suggestions and for his kind help in revising the proofs; and to Mr. Herbert G. Friend for valued and able assistance.

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I.

### INTRODUCTION.

#### CHAPTER I.

## GOUT AND GOUTINESS AND THEIR MANIFESTATIONS.

WE are still unacquainted with the nature of gout, one of the most ancient among the recorded diseases of our race; and, unhappily, the difficulties inherent to the subject have been complicated by those of its nomenclature, the term 'gout' having sometimes been applied to the well-known structural results, at other times to the functional derangement leading to them.

There was a practical simplicity in the terminology used by the ancients; it had the great advantage of clearness. The expressions 'podagra,' 'gonagra,' 'omagra,' 'chiragra,' etc., indicated merely the seat of the painful affection, irrespective of any constitutional factor. The substitution for this nomenclature of the single term 'gout'\* did not simplify matters; it asserted the exist-

\* Introduced by Radulfe at the close of the thirteenth century. Galen (130—200 A.D.) had regarded the tophi as dried accumulations of mucus, gall and blood, and Paracelsus (1493—1541) as a 'mucous essence full of earthy salts,' a 'Tartarus' burning 'like hell-fire.' Sydenham's views (1624—1689) contributed no less than subsequently the opposite doctrine of Cullen to define gout as a constitutional disease. For Sydenham the articular affections and the tophi were as

ence by the side and independently of the articular troubles of a constitutional disease which, even to the present day, it has been impossible strictly to identify, and it even suggested a theory as to its nature. A great part of the literature of gout has since then been devoted to a discussion of this supposed constitutional disease; and its recognition is implied in our present nomenclature.

Modern research has once again thrown the chief stress upon the *local* changes, which alone are demonstrable, and for which the strict use of the term 'gout' has been reserved. Thus, in a limited acceptation, which carefully excludes all unknown and all theoretical matter, 'gout' is simply defined by Sir A. Garrod as 'the group of changes and symptoms connected with the deposition of urate of sodium in the joints and in the tissues.' An extreme development of the same localizing tendency is that which identifies the affection with uric acid, defining it

a means of disposal for the morbid principle of the disease—the materia peccans. Cullen refused to recognise any materia peccans as an essential part of the disease, which he regarded as one of the nervous system, a view which did not enjoy prolonged favour.

The discovery of uric acid by Scheele (1776), and its subsequent recognition in tophi by Wollaston (1787), turned more and more attention towards the local changes, until Garrod's discovery of uric acid in the blood as well as in the joints led to gout being almost identified with uric acid as the essential principle, and as the agent in its localization. Just as in ancient terminology gout did not exist apart from joint affections, so now the cry was, 'Without uric acid, no gout.' Uric acid became, as it were, a criterion for the correctness in any given case of the term 'gout,' which became more closely reserved for the varied manifestation connected, or supposed to be connected, with uric acid. An indirect result of the growth of the uric acid theory was the comparative neglect of the constitutional aspects to which the term 'gout' was less and less commonly applied. We shall see that in a certain measure this deficiency was supplied by the word 'diathesis.'

merely as 'uric acid in the wrong place,' and which excludes the latent constitutional factor on the principle, 'without uric acid, no gout.'

The interdependence of gout and of uratic deposits has been less in question than the precise nature of their relations.

Gout is really made up of the 'uric acid trouble' and of 'something else,' or, rather, in the order of the events, of something concerning which we should like to know more than we do, and, in the second place, of the uric acid complication.

Not many years ago tubercular phthisis, in spite of our familiarity with it in every phase and variety, was an unsolved problem. The results of the disease were obvious; its essence entirely unknown. This is almost exactly our present position towards gout—much familiarity with, and some knowledge of its manifestations, but nothing known of their original cause, from which they may differ as much as tubercle and its life-history differ from Koch's bacillus. What we commonly understand by 'declared gout' may represent late results only, having little in common with the fons et origo mali.

Phthisis was adduced merely to illustrate the needful distinction between the morbid agencies of a disease and their manifest products. Nothing leads us to suspect in gout a parasitic element, though others besides Boerhaave (1668—1738) entertained the view that it was sometimes contagious; indeed, whilst recognising gouty morbid actions totally distinct from the precipitation of uric acid with its long train of symptoms, we hardly trace in gout the complete outline of a disease. Neither need we assume any foreign morbid material. A simple deviation of the natural constituents of the body from their normal

type and function might explain all. We might simply be dealing with a disease of faulty nutrition (using this term in its broadest sense), in which our tissues would suffer in their rate and mode of growth, of function, and of decay. Gout might then be regarded as one of the most striking instances of a long-continued functional disorder, ultimately culminating in structural change; and of the resulting product, the gouty subject, there might be many types, because there are many degrees of gout and of goutiness.

The more liberal use of these terms has been the outcome of closer clinical observation. The first attack of the toe-ache marks a man; not only is he liable to its return, but during the intervals between the attacks he cannot face with impunity various risks to which his health was previously indifferent. He is henceforth a 'gouty' person, and may suffer from a variety of slight gouty ailments, even though he may never have another severe fit of the gout.

An analogous case is that of the son of gouty parents, who may present at a relatively early period a variety of conditions which might be difficult to account for without a knowledge of the family history. In a doubtful case of this kind, where the history cannot be obtained, an acute arthritis supervening at last would, as it were, legalize the position of the nondescript symptoms, and confer upon them a retrospective gouty status.

Uncertainty as to the value of the term is the source of practical, and of even personal, inconvenience, not a few patients resenting the imputation of gout (though to others the impeachment is welcome) if they should not have suffered from any local evidence of its presence; the articular attack, whilst it differs in every point from the changes which lead up to it, being rightly regarded as the

only reliable criterion for gout. Prior to the first articular outbreak, the significance of the clinical events can only be guessed, and their cause is often overlooked or misunderstood.

#### THE MANIFESTATIONS OF GOUT.

The fact is, we know gout only through its manifestations. The *local manifestations*, even at their onset, are bound up with structural changes, which have supplied abundant material for pathological study. The seats of 'local gout' are varied; it occurs in the upper extremity or the lower, in the larger joints or in the smaller ones, though more often in the latter; it may affect the external ear with chalky deposit, or the palmar fascia with Dupuytren's contraction; but in the viscera, except the kidney, the local changes are difficult to trace, though we occasionally gain evidence as to their situation.

With the general manifestations it is otherwise; for long periods the change is in the function rather than in the structures, and the latter afford no object lesson for the pathologist. Nevertheless, in its ultimate stages and in its gravest form, when it has long been complicated with the local accidents, 'general gout' obtains full recognition. In the gouty cachexia of this stage structural change is unmistakably present; but it is of a kind more obvious to the eye in its general aspect of decay than to the finer instruments of research in its details.

We should not, however, assume that gout exclusively resides in its structural manifestations. A man may remain gouty even if some accident should deprive him of a limb, and, with it, of his 'local gout.' He will not long escape fresh inroads and settlements of the enemy, if he should continue to neglect to guard against its approach, nay—sometimes in spite of vigilance itself.

Could we but know wherein consists the difference between this man and one in unshaken health, we should know what gout is.

#### GOUTINESS.

We have still, then, to deal with that earlier period of 'general gout' which pathological anatomy fails to recognise. That this period is not one of health, neither the patient nor the physician needs telling; but how soon they may succeed in identifying the ill-defined cause depends upon their personal experience. A patient may not develop 'local gout' until he has passed through an ordeal of symptoms, which for a time may have afforded equal scope for the shrewdness of observers or for their scepticism.

This important stage of 'general gout' is our opportunity for that better form of cure, prevention. The stage of purely functional disturbance possesses no strict nosological position, but for clinical purposes the term 'goutiness' seems the most appropriate. Goutiness may last for long periods or to the end; but its tendency is to develop into declared articular gout.

The vagueness of the term is not a drawback, in view of the ill-developed character of the conditions to which it applies; its comprehensiveness is an advantage, for their variety often includes minor local changes, such as phalangeal nodules or tophi, etc., the presence of which removes all doubt as to the genuinely gouty nature of the rest. Being a purely clinical expression, it does not appreciably complicate the question; and whilst asserting the gouty complexion of the symptoms, it leaves untouched the obscure problem of the antecedents of gout and of the constitutional basis of the affection.

We may, then, bear in mind provisionally the following varieties:

- I. Gout itself, apart from its manifestations, or the still unknown cause of all gouty phenomena.
- II. Declared gout, or gout associated with definite structural change. This includes two sets of phenomena: (1) The local manifestations, and in particular gouty arthritis, which may be acute and temporary or chronic and permanent; and (2) the general manifestations, among which may be included the acute visceral seizures, but which essentially consist of the chronic changes special to gouty cachexia.
- III. Goutiness, or the condition of imperfectly declared gout; not necessarily associated with definite structural changes (though these may also be present in a minor degree), and usually consisting of varied functional disturbances of a general kind which set up merely clinical symptoms.

#### CHAPTER II.

## QUESTIONS OF NOMENCLATURE.

DIATHESIS, ARTHRITISM, HERPETISM.

THE 'Gouty Diathesis.'—Mere names cannot take the place of facts. The poverty of our vocabulary simply reflects the poverty of our knowledge, and this bids us to be content with the use of the word 'gout,' rather than to risk confusion. From this risk the recently much favoured expression 'gouty diathesis' is not exempt. Its lack of definition and its emptiness have led the present writer to avoid its employment for that of straightforward expressions, such as 'disposition' and 'special liability,' which do not tempt us to create a thought to fit the word.

Various more or less imaginary 'turns or modes' of constitution, which were formerly described as diatheses, have now melted into thin air. The 'gouty diathesis,' which is still with us, has served our literary convenience rather than the interests of pathology. It reminds us of those capacious brackets used by mathematicians for the safe handling of unknown quantities, except that the mathematical formula works towards a solution, whilst 'diathesis' can only perpetuate the problem. Whether the word is intended to express an inherited liability or an acquired tendency, perverting influences or the resulting perversion of the constitution, an explicit statement in each case is indispensable for clearness.

It might, in the first place, be questioned whether a diathesis which is acquired and that which is inherited are likely to be identical. But there are worse objections than this. It is a peculiarity of gout that it attacks individuals of the most different types, habits, and constitutions, some of whom are already the bearers of other diatheses. The supposed 'gouty diathesis' cannot, without strain, be made to fit such opposites as the over-fed, full-blooded, and plethoric, and the thin, half-starved subject, the scrofulous, and the nerve-ridden patient. What can such extremes possess in common by way of disposition? The wonder is, rather, that goutiness should develop in all classes of subjects, irrespective of undoubted constitutional differences.

Above all, there is no finality in the indulgence in 'diatheses'; it grows as a habit. Given an opening for some fresh diathesis, say in connection with the excessive excretion of uric acid, and a 'uric acid diathesis' is forthwith set up. Indeed, this diathesis now claims the domain of gout with a title almost equal to that of the 'gouty diathesis' itself. Yet the two diatheses, though they largely overlap, cannot be fused into one. They are both distinct and well-constituted 'diatheses.'

The 'Uric Acid Diathesis' embraces a great deal more than gout, viz., all other conditions in which uric acid is in excess, whether they are as in gravel, indirectly related to gout, or as in leucocythæmia, absolutely foreign to it. There is, at any rate, something tangible in the uric acid diathesis: it implies a recognisable excess of a chemical substance; but the 'gouty diathesis,' if it means anything apart from inherited delicacy, or from the earliest manifestations of gout itself, is of exceedingly frail construction, and falls to pieces if we endeavour to isolate it from its bearer. Doubtless much of the so-called 'gouty

diathesis' is nothing more than gout itself in its earliest and least obvious form. The confusion arises entirely from the use of a superfluous word, which we can well afford to give up.

'Herpetism' and 'Arthritism.'—The influence of names in perpetuating mere hypotheses is also shown in the extension given to the words 'herpetism' and 'arthritism,' which have been applied by French pathologists to supposed constitutional tendencies or states distinguished by singularly vague outlines. The futility of this nomenclature of the unknown is well exposed by Dr. Lecorché in his criticism of the resulting confusion of ideas.\*

\* 'Or, il est devenu de moins en moins facile de faire la lumière dans le chaos nosologique auquel les médecins français ont imposé cette étiquette. Pour les uns, c'est une diathèse, une manière d'être de l'organisme prédisposant à certaines affections; pour les autres, c'est une sorte de maladie générale analogue à la syphilis, par exemple, ayant des déterminations multiples sur les muqueuses, sur la peau, sur les viscères mêmes; car on décrit une bronchite, une angine, une entérite arthritique. Pour les médecins qui s'occupent des maladies de la peau, tout ce qui n'est pas syphilitique ou scrofuleux est arthritique, et encore existe-t-il des syphilides et des scrofulides de nature arthritique. Pour les médecins des stations hydro-thermales, tout sujet souffrant de douleurs articulaires, musculaires ou nerveuses, est entaché d'arthritisme ; la goutte, le rhumatisme aigu, l'arthrite déformante, les arthropathies de toute nature, ils confondent tout sous cette dénomination commode. Étrange aberration d'un esprit remarquable, Pidoux considère ce beau désordre comme un effet de l'art. "La science," dit-il, "les écoles sont aujourd'hui à la distinction radicale du rhumatisme et de la goutte ; l'art, au contraire, incline à les croire congénères."-PIDOUX, "Qu'est-ce que le Rhumatisme?" Paris, 1861, p. 31.

'Et nous ne parlons pas de ceux qui, sous le nom d'herpétisme, ont voulu créer une nouvelle variété d'état diathésique, variété dont les caractères sont tellement semblables aux manifestations assignées à l'arthritisme que les élèves même de Bazin ont renoncé à faire la distinction.

'On voit que le mot chaos est le terme juste pour caractériser une pareille situation. Comment y faire la place de la goutte? La goutte, With the help of a name these pure concepts acquire an appearance of reality, and further generalizations are based upon them. We find ourselves passing from the substantive to the adjective case, an 'arthritic' or 'herpetic' quality being described even in symptoms and conditions not connected with the joints or with the skin; and we are raised at one step to the height of abstraction when we are told that 'arthritism' may exist without any joint trouble, and 'herpetism' without any skin affection. We agree with Lecorché that 'chaos' is the only word applicable to the result. The disappearance of the three names which head this chapter would be, in the writer's opinion, an unqualified gain.

c'est l'arthritisme, disent les uns; la goutte est une branche de l'arthritisme, disent les autres. La goutte et le rhumatisme sont les deux embranchements d'un même tronc, qui est l'arthritisme, dit Pidoux. Qu'on définisse d'abord l'arthritisme; on pourra discuter ensuite. Pour nous, en attendant, la goutte est une maladie qui se différencie des autres maladies à manifestations articulaires par un excès d'acide urique dans le sang et dans les tissus, et elle n'a aucune analogie avec le rhumatisme, maladie infectieuse.'—' La Goutte et les Maladies Associées.' Paris, 1884, p. 425.

#### CHAPTER III.

## PATHOLOGICAL QUESTIONS.—GOUT AND METABOLISM.

Any attempt to define the word 'gout' inevitably brings up the following questions:

- 1. Does there exist in those whose joints suffer the changes, which all are agreed to call gout, any constitutional morbid process capable of arising or of persisting independently of the articular trouble?
- 2. If any such independent morbid process exists, to what extent can it claim to be regarded strictly as a disease?
- 3. What is its relation to the joint trouble—that of a cause, a complication, or a result? If it be the cause of the arthritis, should it not be regarded as the chief part—nay, the essence of gout?

In simpler terms: Is gout merely a local affection, and are we to restrict the use of the term to the attack of pain and of swelling? Or is it essentially a constitutional affection with local complications? If so, has it any separate existence apart from changes in the joints? Can it exist in a patient in the intervals between the articular seizures long before their first appearance, or long after their cessation? Lastly, what name should be applied to it?

Slender as is the pathological support, we can hardly exclude the notion of a general and constitutional affection.

Our medical language betrays the impression that there is a constitutional background for the local events. We speak of the manifestations of gout. Again, such terms as 'latent,' 'retrocedent,' 'suppressed,' 'and 'visceral' gout can only apply to some internal affection. Swollen joints are not inherited, but we say of gout that it is hereditary. The word 'diathesis' also conveys, though in a nebulous form, the same interpretation.

The clinical evidence in favour of the existence of a constitutional aspect of gout will probably be regarded as sufficiently strong to compensate for the almost negative pathological evidence. Constitutional gout often exists apart from its articular manifestations, which may not evolve till late, or even at all. The verbal difficulty which this admission implies may be lessened by the use of the term 'declared gout' for all cases in which the articular complication is developed; whilst 'goutiness' would conveniently express the varied constitutional disturbances not associated with articular mischief, which are in many subjects the alternative expression taken by the affection.

#### GOUT A PERVERSION OF NUTRITION.

The skin of gouty people, their tissues, the incidents in their clinical history, and their functions, particularly those of the nervous system, all tell the same tale of delicacy, vulnerability, and excessive response to stimulation. The change is a pervading one. The skin is thin and vulnerable; the mucous membranes frail and irritable; the nervous system quick and excitable. Yet we do not attempt to localize the disease in connection with the skin, with the mucous membranes, or with the nervous system. The condition is one affecting the entire body and each cell within it, even the germ-cells sharing in the alteration, and transmitting it to the

offspring. So general a change can only be due to a deep-seated process affecting metabolism itself.

Metabolism.—The simple word 'metabolism'\* conveys to the trained mind the idea of a complex and unceasing exchange between the component parts of the organism, which is the material basis of life. In a restricted sense it is the chemical interaction between the living cell-substance and the soluble substances and juices supplied from the blood to permeate the spongy cellular structure, and ultimately to be gathered again into the blood through the lymphatics.

Metabolism is the agent of growth and of decay; in technical language, it is both 'constructive' and 'destructive.' Both operations are simultaneous, one set of substances being built up, the other broken down. The balancing of these two linked processes constitutes the perfection of health; their complete arrest is equivalent to death; their undue acceleration or delay, or their deviations from the normal type, meaning disease.

Leaving aside the comparatively coarse accidents which may befall the adjustment of the *supplies*, and their eventual absorption and assimilation, the much finer and more intimate elaborations which constitute metabolism proper are essentially of the nature of oxidations. The diseases characterized by faulty metabolic processes form a group to which the name of nutritional diseases or

<sup>\*</sup> This is an instance of the convenience of a dead language in science. The word 'metabolism' is Greek—nearly all our old medical words have been, and all our new words year by year are taken from the Greek. Yet Greek, hitherto an ornament and an element of culture, and now more than ever an intellectual necessity, is taken away from us, and, in the name of educational progress, the great body of the profession is cut off from the sources of medical nomenclature, and from an intelligent use of its own technical terms. Can this policy be right?

diseases of metabolism is properly applied, and to these belong, among others, gout and obesity.

In some of the peculiarities of both affections we trace indications of a slowing rather than of an acceleration of the metabolic changes. This view has been ably put forward by Professor Beneke, and subsequently by Professor Bouchard, under the significant titles of 'maladies par ralentissement de la nutrition' and of 'nutritions retardantes.' But it would be rash at this stage to dogmatize on so abstruse a subject. We must bear in mind that the fault may be not so much in the rate as in the direction which metabolism may assume. In the end-products we certainly have to deal with errors in proportion—too much fat in one case, too much uric acid in the other. This would rather suggest a deviation from the normal chemical routine than a mere alteration in its rate.

### LESSENED TISSUE RESISTANCE IN GOUT.

As regards function, the direct outcome of this intimate derangement of nutrition is a lowered resistance of cells, tissues, and organs. Gout is evidently a disease of diminished resistance, and, in that sense, of debility—an important point to be remembered in connection with treatment.

In the individual case the resistance may be diminished in some special direction, *i.e.*, one organ or system may be specially susceptible, and the goutiness will then lead to well-defined symptoms; or it may remain widely distributed, without special localization, and ill defined in its manifestations.

The joints stand out among all other tissues as least resistant to the gouty influence. Their susceptibility is characteristic of gout, though it cannot be regarded as an exclusive, universal, or absolutely essential feature. Their

loss of functional resistance is shown in their inability to resist the deposition of the urates. The uratic infiltration of those joints which for reasons unknown are specially prone to suffer is the most striking pathological aspect of gout. The tendency to abnormal accumulation and deposition of uric acid, though pre-eminently localized in the joints, is a general feature of gout; whilst uric acid itself is apparently a by-product of the special perversion of nutrition originally mentioned.

## OR PRE-ARTHRITIC STAGE.

The distinction which has been suggested under the names 'gout' and 'goutiness' between two degrees or varieties of the affection is not unsupported by facts. In a large number of subjects, including many who inherit gout, the joint troubles and the uratic deposition are but slight, or occur late; whilst the general constitutional features assume prominence. In acquired gout, the articular and the uratic manifestations are almost invariably the first to appear, and most commonly their advent is acute and unexpected.

In the other set of cases the arthritic development is manifestly worked up to, and gradually evolved. The joints escape for a time whilst gouty mischief is astir elsewhere. This stage of gout may aptly be designated as the pre-arthritic stage. Its often considerable duration and the gouty character of some of the events within it might lead us to regard it as part of the pathological history of all gout, and to expect some analogous evolutionary period in all other instances also; but in acquired gout, if it exists at all, the pre-arthritic stage is certainly not manifest. Further reference will be made to this subject in the Clinical Section.

Declared arthritis, then, should it supervene, serves as a clinical test for the gouty nature of any antecedent abarticular phenomena. The familiarity which may thus have been gained with the latter, aided by the family history, enables experienced physicians to identify their character almost with certainty, even in the absence of the criteria of articular gout. Cases of this kind, formerly described as 'incomplete gout,' throw light upon the natural history of the affection. Its development, in a large number of instances, is not sudden, and its localization in the joints may be long delayed. Meanwhile, general changes occur imperceptibly, which at first are more difficult to seize upon because not confined to any locality; but the general aspect of 'goutiness' does not long escape recognition by the expert, and it conveys the undoubted impression that the general nutrition has suffered, a conclusion which becomes obvious to all in the extreme condition known as 'gouty cachexia.'

#### CHAPTER IV.

### CLINICAL QUESTIONS.

THE RELATIVE PREVALENCE OF GOUT AT THE PRE-SENT TIME.—THE ATTENUATIONS OF GOUT.

PECULIAR interest attaches to the question whether gout has shown any variation in its type since the earliest times, and what differences may be traced between gout in former days and the affection such as we now witness it. The geographical or climatic and the ethnical factors in disease have received increasing attention; but a systematic study of the variations wrought by the progress of time has yet to be undertaken.

Gout is certainly as ancient as civilization; and so far as we can identify them in the accounts handed down from remote ages, the ætiology, the leading symptoms, and the outward characters of the articular gout of the ancients were practically the same as belong to gout in our own times; but of its relative prevalence in antiquity we have no means of judging. The ultimate lesions of gouty arthritis and its pathology are presumably as immutable as those of osteo-arthritis, a disease the characters of which may be studied in specimens which have reached us from prehistoric times, and the same is probably true of any visceral lesions akin to the arthritic.

Nevertheless, that minor changes may have occurred with the lapse of time there is good reason to believe.

Indeed, they may be expected in a disease essentially conditioned by the mode of life. In its clinical types, in its duration, and in its relative mildness or severity, there is room for much variation. Whilst, then, the essential pathological features are probably the same now as ever they were, all the rest in gout is variable, and more especially the mutual relation and degrees of the two phases.

The history of abarticular gout in the distant past cannot be traced with any certainty; but in connection with less remote periods the inquiry can be conducted with some definiteness, and it possesses practical interest, since the remedies and the doses used by our fore-fathers might not be necessarily suitable for the present generation.

#### CONTEMPORARY GOUT AND GOUTINESS.

Gout being to a large extent a manufactured product of civilization, and being influenced more than most other affections by inheritance, conditions of life capable of impressing peculiarities upon the organism may be expected to affect in a direct manner the liability of subsequent generations. The modifying influences special to modern times can only be briefly indicated. Our luxuriousness of living vies with that to which the gout of the ancients has been attributed; but in addition profound changes have taken place in the social and economical conditions of the last few generations, none of which is probably so important in connection with gout as the agglomeration of the population in large towns.

Moreover, the present century has called into operation previously latent forces of Nature. The scheme of life is complicated by new agencies; the storage and the liberation of nerve energy are both altered in their rate and in their amount; wear and tear which is saved by anæsthetics

and narcotics is hastened by steam and electricity. Our habits and occupations, our expenditure of energy, our food, have all undergone alterations. In a word, the artificial conditions which tend to modify the reaction of the organism have grown at a rate previously unexampled; and although it were difficult to prove that we differ in any wide measure from generations which have preceded us, a belief prevails that in certain directions, particularly in that of the nervous system, the influence of our surroundings has not been inoperative,\* and that the quality of the vital reactions to stimulation has undergone slight modifications.

Passing, however, from this large and debatable subject, we may point to definite influences modifying in a calculable degree the prevalence and the type of the affection. Indeed, within the recollection of those who can look back far enough, perceptible changes have taken place in the prevalence of gout, in the type of the gouty attack, and in the peculiarities of the gouty state.

# THE ATTENUATION OF ACQUIRED GOUT.

The relative *prevalence* of each of the diseases of middle age is now increased by the accession of lives such as were previously cut short by typhus, typhoid, diphtheria, etc. Thanks to modern hygiene and preventive medicine, the gouty period of life is now reached by these vulnerable constitutions, among whom many are prone to goutiness or the bearers of a gouty inheritance, and therefore likely to establish a gouty posterity.

The type of the affection has also been exposed to modifying influences in the individual and in the race. The

<sup>\*</sup> The views of Dr. Pye-Smith, which differ slightly from the above, might be read with interest. Cf. Lumleian Lectures on Ætiology: Harveian Oration and Memoir. London: J. and A. Churchill, 1895.

diffusion during the two last generations of sounder views on hygiene and diet must have checked the severity of acquired gout, as well as the strength of the predisposition transmitted to the offspring. Among the classes most liable to the disease, a broader appreciation of the evils of gout has led to greater prudence in respect of food and beverage. A great share in this result is doubtless due to the enlightened action of the profession, whose almost unanimous advice in respect of the rules of diet has obtained increasing attention.

Observation confirms the correctness of this surmise. Physicians of mature experience no longer witness the violent attacks of gout with which they had been familiar in their earlier days. On the other hand, they can trace no decrease, but rather an increase, in the prevalence of goutiness—if under that conveniently vague and comprehensive term we include those unstable states and those ill-developed manifestations for which it would be hard to assign a nosological position except under the heading of gout.

# THE ATTENUATION AND THE FREQUENCY OF GOUTINESS.

This change to a milder type has not been confined to the articular seizures of acquired gout. With an increased prevalence, or, at any rate, with an increased recognition of the abarticular forms, we note also their lessening severity. A larger proportion of cases present mere attenuations, not always gouty at first sight, but readily identified as such in connection with their attendant circumstances, with their exciting causes, with their occurrence at certain seasons, with their retinue of collateral affections, and with the constitutional aspect of the patients. Without these helps many a case might

be overlooked. In certain families some members inherit gout badly, others slightly, others not at all; the slighter degrees of inheritance are perhaps observed with increasing frequency, and goutiness is becoming relatively more common than declared gout.

In this circumstance, and in the general mitigation of all the arthritic manifestations, we see a hopeful sign. The possibility of an ultimate extinction of the bias in gouty families is denied by some authorities, but we should not forget that by the side of the tendency to a reproduction of morbid parental peculiarities there is a yet stronger tendency in Nature to reproduce the healthy type of the race in each successive generation.

Meantime, one of the features of contemporary practice is the prominence allotted to the gouty factor, and the frequency with which it is held to complicate or modify other affections.

The tendency to attribute to gout a variety of ailments of an obscure complexion, arising in those likely by inheritance or by habit of life to be eventual victims, is by no means novel. Even forty years ago many diseases whose clinical features are now quite familiar were in those days unknown. Strange symptoms had to be explained under some of the available heads of disease, and gout came in for a large share of vicarious responsibility.\* Errors in

\* Even so recently as 1854 Sir Spencer Wells wrote as follows in his 'Practical Observations on Gout and its Complications, and on the Treatment of Joints stiffened by Gouty Deposits' (John Churchill, 1854):

'Any attempt to describe the nervous diseases of females caused by gout would lead to an enumeration of almost all forms of their diseases, especially those usually considered as hysteric. The intestinal derangements, with tympanitis, neuralgia, or colic, the hysteric pain in the right epigastrium, the cardialgia and gastrodynia, the hysteric vomiting and epigastric spasms, the morbid sensibility of the pharynx and fauces, hysteric palpitation, asthma, or bronchitis, diagnosis are probably much less common nowadays; at any rate, the reproach of unduly extending the domain of gout is much less deserved by the present than by former generations of physicians. Many of the affections which Musgrave and his successors described as gout are now identified as separate organic or functional diseases.

The converse is also true, though probably in a less degree. The gouty character of not a few affections may have been overlooked in the past,\* and instances of the same oversight are not unknown in contemporary practice.

loss or alteration of the voice—some forms of hysteric paraplegia or hemiplegia, more or less complete—chorea or tetanus—some of the curious paroxysmal affections observed in hysteria, and all the varieties of neuralgiæ and simulated inflammation, commonly called hysteric, frequently arise from the presence in the blood of the impurities which are the true characteristics of gout.'

In that list there are names we can now relegate outside the pale of gout. At the present time there are still unrecognised diseases, and of some of these, perhaps, we may still erroneously refer the symptoms to gout; but their number cannot be great. Yet the concourse of conditions directly or indirectly referred to the influence of gout is truly remarkable.

\* This aspect was dwelt upon by Laycock in connection with hysteria:

'Of the many cases related by authors as anomalous disease, by far the greater portion were connected with a gouty diathesis, as indicated both by the formation of calculi, by the occurrence of regular paroxysms of gout, and by the descent of the individual from gouty ancestors; they are cases, in fact, which would have been better understood and better treated if they had been termed "anomalous gout"; but as the subjects are young females, they are, of course, set down as "anomalous hysteria" ('Nervous Diseases of Women,' p. 163, quoted by Sir Spencer Wells, *loc. cit.*, p. 163).

Since that date the rise of the pathology of the nervous system has led to the domain of hysteria being considerably broken up; but it cannot be said that any appreciable share of it has fallen to gout. These lines are quoted as illustrating the unavoidable fluctuation in the nosological position of symptoms, so long as they lack a strict pathological explanation. We are not exempt from the same uncertainties, though less and less exposed to them.

Granted, then, a large retinue of kindred states, we must still carefully check them as to their absolute identity with gout. We are still liable to similar mistakes. Although many diseases have been identified and their manifestations excluded from the gouty connection, the supply of newly-observed phenomena awaiting an explanation is constantly kept up by the searching modern methods of clinical study; and immature gout may be at times erroneously credited with the causation of novel symptoms. In less than forty years deductions may have to be made from our present list of so-called gouty manifestations, though probably not as numerous as those we now can make in the review of the 'gouty' symptoms of forty years ago.

#### CHAPTER V.

## THE GENERAL ÆTIOLOGY OF GOUT.

THE general ætiology of gout as regards heredity, age, sex, climate, and conditions of life is fairly well known.

At least half the cases of gout are *inherited*. This is about the proportion worked out by Sir A. Garrod. Scudamore found a ratio of 309 to 523, and other observers a still higher proportion; a few only estimating it at one-third.

Most commonly gout is inherited from the father. Maternal gout, however, being less frequently of a declared type, may often have been overlooked in statistics; this might partly account for the wide differences between the various estimates. It has long been known that the later offspring is more liable than the earlier, and Mr. J. Hutchinson\* draws attention to the fact that the last born of a gouty progeny are more likely to develop the affection early and to suffer severely.

Gout is undoubtedly modified in transmission. This is a natural consequence of the greater delicacy of the offspring, and of the inheritance of gouty structural peculiarities from progenitors whose own gout, if acquired, may have been grafted on a robust constitution. Gout, in the weaker subject, could not develop on the same lines as in the stronger one.

<sup>\* &#</sup>x27;The Hereditary Transmission of Gout,' Medical Times and Gazette, May 20, 1876.

Quite independently of this general modifying influence, there are curious inconsistencies and interruptions in the hereditary transmission of the disease. Some children may escape entirely, while others are attacked; or a generation may be spared by the disease, which may return in the ensuing one. Yet more strange are the alternations frequently observed in the type of the disease, the arthritic being succeeded, for one or even two generations, by the cutaneous, the calculous, the nervous, or some other visceral form, after which arthritic gout may again occur. These observations open up wide speculations connected with atavism, a subject upon which Dr. Mortimer Granville\* has supplied some interesting remarks.

Age is a leading factor. The extremes of age are almost exempt; early growth, which monopolizes energy, and senile decay, in which it is almost extinct, both overrule that deviation of the energies of nutrition which we consider to be at the root of gout. Gout begins at that period of manhood when the first restlessness of youth is wearing off, and gives way to a greater appreciation of things, and to a systematic enjoyment of life. The greater number are attacked somewhere before forty. Patissier+ found thirtyfour to be the average age of onset for inherited gout, and thirty-eight for the acquired form. Not a few, however (as many as 85 in a series of 515 collated by Scudamore), begin their gouty history between twenty-five and thirty; but before twenty gout is exceptional, and earlier cases should be reckoned among the curiosities of gout. Scudamore mentions a case at each of the unusually early ages of eight, twelve, fifteen, sixteen, seventeen; and similar instances are scattered through literature. It was the

<sup>\* &#</sup>x27;Notes and Conjectures on Gout,' Baillière, Tindall and Cox.

<sup>†</sup> Quoted by Rendu, loc. cit., p. 174.

original observation of Hippocrates that gout does not occur in the young ante usum veneris. Sydenham says: 'Neither have I seen gouty minors or gouty children. The most I have observed is a slight foreshadowing of a future attack, and this has been in the younger branches of gouty families.' At the other extreme of life, the evolution of gout at ninety in a case mentioned by Sir Dyce Duckworth is probably the most senile instance on record. Garrod mentions several cases occurring after seventy, and Blackmore also noted a first attack at seventy-eight. Scudamore's list does not mention any cases after sixty-six, and only ten of his cases occur after sixty.

Sex plays an important part in ætiology. Gout is quite exceptional before the menopause, as was laid down by Hippocrates. Sydenham had also observed that 'gout attacks women but rarely, and then chiefly the aged and the masculine. Where you have symptoms of gout in slender females, they are really the symptoms of hysteria, or else of rheumatism imperfectly eliminated.' We shall dwell elsewhere on the fact that even after the menopause goutiness is much more common in women than declared gout.

Social position fosters the tendency to gout in the measure of the luxuriousness and muscular inactivity which it brings, and of the inherited proclivity often attaching to it. We are reminded of this by Sydenham's lines: 'For humble individuals like myself, there is one poor comfort, which is this, viz., that gout, unlike any other disease, kills more rich men than poor, more wise men than simple. Great kings, emperors, generals, admirals, and philosophers have all died of gout. Hereby Nature shows her impartiality, since those whom she favours in one way she afflicts in another. A mixture of good and evil pre-eminently adapted to our frail mortality.'

Climate and season also markedly influence the prevalence

of gout. The immunity of tropical and sub-tropical countries, and the greater prevalence of gout in some Northern countries, harmonize with the common experience that cold and damp are among the determining causes. Nevertheless, a few remarkable exceptions cause us to doubt whether latitude and temperature alone are adequate to explain the differences observed. In Great Britain, the North has enjoyed almost complete immunity\* for centuries during which gout has been prevalent in England. In the northern section of the European continent, where winters are much colder and more protracted than in England, gout is not prevalent. In Italy the South is said to be its special home; and this was attributed by the late Professor Cantani to a direct inheritance from the Greeks and the Romans. Ancient Rome was another striking exception. India, where gout is unknown among the indigenous native tribes, confers immunity upon British residents, and also a protection from attacks upon those who have been sufferers from gout, but only on condition that their diet is regulated by prudence. The Parsees, who are, like ourselves, an imported race, suffer in a marked degree; and it is significant that they are large consumers of meat. Again, the considerable immunity from declared gout enjoyed by Canada and the United States, in spite of their northern latitude and cold winters, is not to be explained as a result of latitude or temperature. Rendu, in his able analysis of the geographical distribution of gout (loc. cit., p. 166), suggests that behind the influence of climate we probably have to deal with race, and especially with the conditions of social life, and, above all, with diet.

<sup>\*</sup> Dr. Hoffman informs me that this immunity no longer exists in he northern counties of England. During his period of practice in Northumberland, he met with many cases.

The greater prevalence of gout in spring and in autumn has never been thoroughly explained. It cannot be satisfactorily accounted for by the severity of the cold or of the heat. More probably it is connected with disturbances of the liver set up by abrupt variations in the wind and weather.

The exact share attributable to racial proclivity is difficult to estimate. The Anglo-Saxon and the Dutch stand, in respect of gout, in a marked contrast to the Scotch and to the German or Scandinavian. Both England and Holland are remarkable for the humidity of their climate and for their liberal dietary. On the other hand, Scotland and Ireland, the recognised homes of frugality, are no less humid than England, whilst Germany enjoys a relatively dry climate. Here, again, the dietetic factor seems to predominate over the climatic and the racial. As a fact, races so far removed from the regions of prevalence of gout as even the African tribes have furnished instances of gout acquired in the individual after emigration, owing to rich living. The Arabs in the palmy days of their mediæval empire were also addicted to gout, but are now almost entirely exempt.

The general conclusion must be, that no race and no climate can claim to be absolutely exempt from the risk attaching to indulgence in luxurious habits and excess in diet, and that the immunity enjoyed by the tropical countries is in a large measure explained by the activity of cutaneous excretion, and, above all, by the fact, tersely expressed by Rendu, that 'these are countries in which we cannot survive unless we are frugal.' More potent, then, than climatic and racial peculiarities are the habits of the individual.

Temperament may, to a certain extent, determine the type of gout, but gout is not the monopoly of any special

temperament. According to Rendu (loc. cit., p. 176), sthenic arthritic gout occurs in the full-blooded; spare and nervous subjects are liable to the neuralgic, neurotic, and neuropathic manifestations, including asthma and other spasmodic forms of visceral gout; whilst bilious subjects would suffer from the dyspeptic and hepatic ailments, and would be specially predisposed to hæmorrhoids. We have it on Scudamore's authority that the gouty often present a decided tendency to obesity—according to his tables, in the proportion of 126 to 156.

The influence of diet and beverage is discussed in a separate chapter. Acquired gout is developed on a mixed dietary, with liberal meat supplies seasoned with alcoholic beers and wines. In inherited gout the same diet will readily call forth the manifestations, but they may also break out on a diet almost exclusively vegetable, and in the absence, or with the utmost care in the use, of alcoholic stimulants.

A life of physical inactivity is a potent factor in bringing about general gout. Intellectual labour and mental shock are also recognised causes; and it should be noted that they are also operative in diabetes, gravel, and biliary lithiasis. 'Sometimes also serious study and prolonged meditation have increased the evil. This they have done by diverting the volatile spirits from their proper function of assimilation' (Sydenham). In a word, all physical and nervous depressing influences have a share in predisposing to the malady.

# THE THEORIES OF GOUT.

#### CHAPTER VI.

### BRIEF GENERAL SKETCH.

THE multiplicity of our theories argues their relative failure. None have covered the whole ground. Yet each of them, being based on pathological or clinical observation, contains some instalment of the desired solution. Their agreement or conflict may help the elucidation of various doubts; and, if nothing more, we may learn from them that every attempt to identify gout with any of its organic developments has proved futile.

The early history of pathology is made up of successive oscillations between two great theories—the 'humoral' and the 'solidist'; and in the case of gout the discussion has lasted almost to the present day. It is now obvious that no pathology can be built on so exclusive a basis. The fluids and the solids of the living body are so closely bound together that, until released from their union by death, they are inseparable, and even disease is dependent upon their association. However much modern theories may differ, they are all humoro-solidist.

One of them, however, the nervous theory as it was taught by Cullen, draws more closely than the rest towards the idea of solidism.

Another theory inclines strongly towards humoralism, of which it is the modern expression; it assumes that the blood is vitiated through the defect or disturbance of the secretions, especially the hepatic and the digestive secretions. This was the view of Sydenham; and within our own time the contamination of the blood has been further traced by Murchison in his studies on lithæmia to the admixture of faulty secretions from the liver and digestive organs, and by Garrod to a retention of uric acid, owing to its defective elimination by the kidney.

The 'Humoral' and the 'Nervous' Theories.—In earlier days, when the mysteries of nerve life and activity were unrevealed, and the yet more elementary function—that of which one of our greatest modern statesmen once said, 'Everything depends upon the circulation'—was not dreamt of whether as regards the blood or the lymph stream, the alimentary function was within easier reach, and occupied a larger place in the theories of the day.

The fluids found in the alimentary canal, in the vascular system, in the secreting and excreting glands, and in the tissues themselves, were regarded as the agents of disease. This was the humoral theory in its crude and exclusive form; but a great deal of it was true, and has lasted. Indeed, in the latest theory, the primary humoral aspect of faulty nutrition has been worked in by Sir Dyce Duckworth with the secondary dystrophic aspect based upon disordered innervation.

Stahl, who in his day played the part of a reformer in pathology, was the first to refuse allegiance to the humoral doctrine, of which Sydenham had been the last great representative. He endeavoured to trace the disease to the disordered activities of the organism. Cullen, adopting his teaching, carried it to its ultimate conclusions. He completely denied all share to a morbific material,

and attributed the production of gout to abnormal functions of the nervous system. He may be regarded as the chief exponent of a purely nervous theory. His views were too uncompromising to obtain a lasting hold on medical thought. Nevertheless, they had done service in effectually breaking through the old tradition, and in demonstrating the fallacy of the opposite extreme.

After a period of perplexity and doubt, the gradually reasserted influence of Sydenham, the discovery of the presence of uric acid in the gouty concretions by Wollaston, and the increasing importance attached to it, slowly paved the way for a modified humoral theory, which almost identified the *materia peccans* with uric acid.

The exposition of these views was the signal for a revival of the claims of the nervous theory, no longer, however, in the original vitalist form, but as a compromise with and an addition to the henceforth undeniable humoral factor. The tendency in late years to associate a nervous influence with the chemical changes has great significance in connection with the vast progress of clinical observation and analysis.

### THE URIC ACID THEORY.

Garrod's researches form the turning-point in the history of the pathology of gout, by substituting for pure hypotheses some definite facts, and, above all, a demonstration of the abnormal presence of uric acid in the blood and in the tissues of the gouty. Since then the uric acid side of the pathology of gout has claimed an increasing share of attention, both in the laboratory and clinically.

The conception of a uric acid dyscrasia, upon which the modern views of gout are so largely based, is almost exclusively humoral. There is, however, from the humoralist standpoint, a curious inconsistence in the fact that the

mischievous property is in this case identified with a solid, the sodium biurate crystal. So long as uric acid is in solution in the blood or the juices no gouty trouble ensues; but with its precipitation in or about the joints, and in other situations as biurate, it becomes harmful.

Another view more consonant with pure humoralism is that taken by Dr. Haig. Whilst not denying a mechanical power for harm to uric acid in the crystalline form, he insists on the deleterious action of uric acid when it happens to be circulating in the soluble state; and he has described various results, not in themselves gouty, but many of them analogous to gouty phenomena, as a result of this influence. The development of Dr. Haig's views might be identified as the toxic uric acid theory of gout, in contrast with the other aspect of the uric acid theory, relating to the crystallized salts of uric acid, which might be identified as the mechanical uric acid theory of gout.

Lastly, Ebstein has combined the two views, and, as will be elsewhere explained, has conceived a double and reciprocal influence—toxic on the one hand, mechanical on the other—between the tissues and the biurate. This view we may refer to as the mechanical and toxic uric acid theory.

Observations and discussions as to the behaviour of uric acid and of the biurate were a comparatively simple matter, these substances presenting themselves for inspection, and being accessible to chemical investigation. A much more difficult question, 'Why does the biurate occur in the wrong place and in abnormal quantities?' is that to which investigators have hitherto failed to give a satisfactory answer. The elementary factors of this problem are wanting, for it is still debated whether there is an excess in the production, or merely an undue storage of uric acid. Overproduction is represented by Haig's

theory of faulty alimentation, retention by Garrod's views, which have found favour ever since their publication. Garrod does not altogether discard the idea of overproduction; he traces in the gout of the wealthy, free-living subject the excess of uric acid to an excess in the supplies; but he points to the poor man's gout as probably brought about by retention only. In all cases, however, retention is the determining factor of the attack.

The Theory of Renal Block .- An excess of uric acid in the blood, coinciding during the attack with a diminution in the urine, favoured the assumption that the uric acid was hindered in its escape through the normal channels of excretion. The obstacle to excretion was further assumed to reside in the kidney; but its precise nature has never been made clear. This alleged renal block is the more mysterious since commonly no morbid change can be detected in the kidney, and the renal inability to excrete uric acid whilst other substances are excreted is neither absolute nor lasting. Any defect would have to be regarded as functional rather than organic, and, moreover, most ephemeral. In spite of these difficulties, the theory of renal impermeability has been very largely adopted, and is still almost universally held to be the best available explanation.

The strength of Sir A. Garrod's position had been its strict limitation to the province of uric acid. His philosophical reticence as to any more remote element in the disease drew the attention of other writers more definitely to those pathological aspects which appeared to have suffered neglect, and called forth rejoinders by Gairdner, Barclay, and Parkes. The views expressed by them possess great importance, but they failed to make much impression at that time, for they were merely inferences from clinical observation, and had not then the support

of any physical method of demonstration, such as Sir A. Garrod was able to put forward.

The thoroughness of Garrod's work was such, that for upwards of thirty years it called for neither correction nor addition. At last, within a recent period, it has borne further fruit: the chemistry of the uric acid compounds has been explained by Sir W. Roberts' admirable investigations. And, again, Horbaczewski has led the way of discovery into the previously impenetrable question of the derivation of uric acid.

Meanwhile purely clinical research had not been at a standstill. Various observers successively criticised Sir A. Garrod's statement of the subject from the standpoint of the nervous theory. The French idea of diathesis throve on the rapid growth of the new science of neurology until the nervous theory was fairly revived, and this is again presented to us by Sir Dyce Duckworth in his treatise on gout, although the uncompromising position of Cullen, who denied the existence of any morbific matter in the process of gout, is not again taken up.

Gout might also be viewed as a disease of faulty nutrition. An excessive production of uric acid in gout was easily explained, so long as it was postulated that uric acid was a mere stage in the series of oxidations of which CO<sub>2</sub> and urea were the ultimate products. For an excess of uric acid two conditions were held to be requisite: a glut of nitrogen, that is, surfeit of nitrogenous supplies, and a defect in oxidation.

It has been shown long ago by Lehmann that the amount of uric acid and of urea were increased by an animal diet. On the other hand, it was assumed that the proportion between the uric acid and the urea would be dependent upon the amount of exercise, and that exercise would increase the proportion of urea, and diminish

that of uric acid. More recent investigations have shown that neither the alleged facts nor the arguments based upon them are absolutely correct.

Gout is not altogether a disease of alimentation. It is not an intoxication by meat analogous to ergotism produced by diseased rye. Human subjects may eat meat largely, nearly as exclusively as carnivora, and not have the gout. It is not the animal food as such, but the behaviour of the living protoplasm towards the nutritive juices, especially, though not exclusively, those derived from animal food, which comes into account. The nutritive intracellular activities may be exuberant or depressed, or perhaps of the wrong kind. It is with these aberrations that gout would seem to be associated; and gout might be regarded as a disease of faulty nutrition.

The most elaborate tissues and functions being the most dependent upon a perfect nutrition, the nervous system must be among the earliest to suffer under faulty nutritional conditions. An instance of this is seen in myx-edema. In gout the nervous phenomena are well to the front, and many of them are the expressions of the nutritional upset.

Faulty innervation contributes largely to the list of neuroses and functional visceral crises. By reason of the leading position of the nervous system, its disturbances are reflected to the entire organism. Its directing power for metabolism may even be turned into a means for disturbing metabolic processes in the direction of the gouty change. Indeed, an incomplete study of the matter, in which the original error of metabolism was overlooked, might suggest the idea that gout was primarily a disease of the nervous system. It is in that way that the nerve theory of gout has originated.

In conclusion, we still notice two great tendencies: the

modified solidist, in that theory which Sir Dyce Duckworth so happily terms 'the neuro-humoral theory'; and the modified humoral, in Garrod's renal and uric acid theory. A humoral influence is admitted by all, but the positions of importance are variously bestowed upon the nervous system, upon the disturbed chemistry of the organism, or upon its final gouty product, uric acid.

The foregoing is an incomplete sketch of some of the ideas which, variously combined or associated, have served to build up the manifold theories of gout.

A brief review of the theories themselves may be of service. Although their diversity reflects the extent of our ignorance, from each of them something may be gleaned as from a keenly thought-out interpretation of observed facts; but much more may be gained from their joint consideration, so far as they can be compared. Some of them deal only with the pathology of the arthritic phase, others mainly with the ætiological factors which lead up to that phase; in a third group the two subjects are considered jointly, sometimes with some degree of confusion, and we are left to differentiate between them.

#### CHAPTER VII.

### THE CHEMICAL THEORIES.\*

GARROD'S THEORY OF URIC ACID EXCESS AND OF RENAL INADEQUACY.

Pathology remains indebted to Sir A. Garrod† for the central facts which have been the starting-point of all subsequent investigations, and are the acknowledged basis

\* Sir W. Roberts' investigations and opinions will be considered in the pages devoted to the *Chemistry of Gout*.

† The circumstance that uric acid, discovered by Scheele in 1775 in urinary calculi and in urine, and identified in gouty concretions by Wollaston in 1797, had subsequently been regarded by clinical observers as the constant accompaniment of the disease, does not in any way detract from the value of the proof given by Sir A. Garrod of the absolute relation of cause and effect.

The way in which the presence of uric acid in the blood was demonstrated is matter of history, but we cannot refrain from describing it in the discoverer's own words:

'I have named the process the "uric acid thread experiment," and it is thus performed: Take from one to two fluid drachms of the serum of blood, and put it into a flattened glass dish or capsule; those I prefer are about three inches in diameter, and one-third of an inch in depth, which can be readily procured at any glass-house; to this add ordinary strong acetic acid, in the proportion of six minims to each fluid drachm of serum, which causes the evolution of a few bubbles of gas. When the fluids are well mixed, introduce one or two ultimate fibres, about an inch in length, from a piece of unwashed huckaback or other linen fabric, which should be depressed by means of a small rod, as a probe or point of a pencil. The glass should then be put aside in a cool place, until the serum is quite set and almost dry; the mantelpiece in a room of the ordinary temperature,

of all chemical theories on gout. Excess of uric acid in the blood is the immediate precursor, and its deposition in the tissues in the shape of crystalline urate of sodium is the chief feature of the local manifestations, of the disease.

The excess of uric acid, though admitted to be partly due to an increased formation, is particularly identified by Garrod with an imperfect removal from the blood. At this point theory begins.

Structural changes in the kidney are the too frequent, if not the ultimately inevitable result of inveterate gout. At the onset of the disease none have hitherto been found, except those sometimes brought about by some independent affection. The kidneys being healthy in structure, they might, nevertheless, be at fault in their function; and it is this view that Sir A. Garrod has advocated. According to him, a reduced efficiency of the kidney in clearing the blood of its uric acid is the first step that can be identified in the process of disease.\*

or a bookcase, answers very well, the time varying from thirty-six to sixty hours, depending on the warmth and dryness of the atmosphere.

<sup>&#</sup>x27;Should uric acid be present in the serum in quantities above a certain small amount noticed below, it will crystallize, and during its crystallization will be attracted to the thread, and assume forms not unlike that presented by sugar-candy upon a string, as shown in Plate V., fig. 5,  $\alpha$ , b, c. When in the dark field under polarized light it has an appearance represented in the woodcut (Fig. 6). To observe this, the glass containing the dried serum should be placed under a linear magnifying power of about fifty or sixty, procured with an inch object-glass and low eyepiece, or a single lens of one sixth of an inch focus answers perfectly. The uric acid is found in the form of rhombs, the size of the crystals varying with the rapidity with which the drying of the serum has been effected, and the quantity of uric acid in the blood. To ensure perfect success, several precautions are necessary' ('A Treatise on Gout and Rheumatic Gout,' pp. 86, 87, third edition. London, 1876).

<sup>\*</sup> It is interesting to note that Charcot has pointed out that in early interstitial nephritis, whilst the solubility of urea ensures its ready

The grounds upon which he bases this conclusion are experimental and clinical:

'The results of these experiments on the condition of the blood and urine prove that uric acid is not a product of the action of the kidneys, as frequently supposed, but is merely excreted from the system by these organs. They also appear to indicate that the excreting function of the kidneys with regard to the solid portion of the urine is not a simple one, but that urea and uric acid are separately eliminated; also that one of these functions may be impaired or destroyed, the other remaining entire. It appears also probable that, as in albuminuria, the urea-excreting function being chiefly impaired, we find a vicarious discharge of urea in dropsical effusions, so in gout the uric-acid-excreting function being defective, chalk-like deposits are produced by a similar vicarious discharge of urate of soda.'

'Gout would thus appear, at least partly, to depend on a loss of power (temporary or permanent) in the uricacid-excreting function of the kidneys; the premonitory symptoms, and those also which constitute the paroxysm, arising from an excess of this acid in the blood, and the effort to expel the *materies morbi* from the system. Any undue formation of this compound would favour the occurrence of the disease, and hence the connection between gout, gravel, and calculus; hence also the influence of high living, wine, porter, want of exercise, and other like causes, in inducing it.'

'This hypothesis also explains two facts, which have been regarded as militating against the humoral pathology

escape, various other substances fail to pass through the kidney. He noticed that gouty urine did not yield after administration of turpentine the characteristic odour of violets ('Leçons sur les Maladies du Foie et des Reins,' p. 320; 1877).

of the affection, namely, its hereditary nature, and its frequent occurrence in low states of the system; for we can understand that the peculiarity of the kidney with reference to the excretion of uric acid may be transmitted, and likewise that when the function in question is permanently injured, it will not require an excessive formation of this acid to cause its accumulation in the blood' ('Med. Chir. Trans.,' 1848; 'Gout and Rheumatic Gout,' pp. 272, 273).

'My present experience on the subject shows that in the earlier stages of acute gout the urine is scanty, and the uric acid, measured by the twenty-four hours' excretion, diminished; that the acid is thrown out in much larger quantities as the disease is passing off, and that then amounts even above the patient's daily average may be excreted, forming the so-called critical discharges; that after a time the uric acid is again lessened, although not to the extent observed prior to or at the commencement of an attack' (loc. cit., p. 133).

Urea, the most important of the renal secretions, was found by Garrod not to be markedly reduced in quantity in the urine.

Briefly stated, Garrod's theory rests on the following views:

- 1. The accumulation of uric acid in the blood, which is a necessary antecedent of gout, is due to a functional renal defect, which may be inherited or acquired.
- 2. The local deposition of urate of sodium, howsoever determined—and its ætiology includes the operation of all those causes which lead to a diminished alkalinity of the blood, and thus to an easier precipitation of the uric acid, as determining agents for the attack—is the specific cause of the local inflammation, no other affection being accompanied by a deposition of urate of sodium in the tissues.

3. The local inflammation has a curative effect at large, inasmuch as it seems to destroy the urate of sodium in the blood of the inflamed parts.

Sir A. Garrod gives a complete summary of his opinions in the following propositions:\*

'First, in true gout, uric acid, in the form of urate of soda, is invariably present in the blood in abnormal quantities, both prior to and at the period of the seizure, and is essential to its production; but this acid may occasionally exist, at least for a time, in the circulating fluid without the development of inflammatory symptoms, as in cases of lead-poisoning. Its mere presence, therefore, does not explain the occurrence of the gouty paroxysm.

'Secondly, the investigations detailed in the chapter on the "Morbid Anatomy of Gout" prove incontestably that true gouty inflammation is *always* accompanied with a deposition of urate of soda in the inflamed part.

'Thirdly, the deposit is crystalline and interstitial, and, when once the cartilages and ligamentous structures become infiltrated, remains for a lengthened time, often throughout life.

'Fourthly, the deposited urate of soda may be looked upon as the cause, and not the effect, of the gouty inflammation.

'Fifthly, the inflammation which occurs in the gouty paroxysm tends to the destruction of the urate of soda in the blood of the inflamed part, and consequently of the system generally.

'Sixthly, the kidneys are implicated in gout, probably in its early, and certainly in its chronic stages; and the renal affection, possibly only functional at first, subsequently becomes structural; the urinary secretion is also altered in composition.

<sup>\*</sup> Loc. cit., pp. 274, 275.

'Seventhly, the impure state of the blood, arising principally from the presence of urate of soda, is the probable cause of the disturbance which precedes the gouty seizure, and of many of the anomalous symptoms to which sufferers from gout are liable.

'Eighthly, the causes which predispose to gout, independently of those connected with individual peculiarity, are either such as produce an increased formation of uric acid in the system, or lead to its retention in the blood.

'Ninthly, the causes exciting a gouty fit are those which induce a less alkaline condition of the blood; or which greatly augment, for the time, the formation of uric acid; or such as temporarily check the eliminating power of the kidneys.

'Tenthly, in no disease but true gout is there a deposition of urate of soda in the inflamed tissues.'

# RALFE'S THEORY OF LESSENED ALKALINITY OF THE METABOLISM.

Diminished alkalinity of the blood must promote the precipitations of uric acid, even though the production of the latter be not excessive or its renal excretion diminished.

Defective elimination by the kidney has yet to be proved. The first step would be an accumulation in the blood of acids and of acid salts, and associated with this a failure of the tissues to reduce the uric acid, as occurs in health; the next step, a precipitation (favoured by acidity) of uric acid, on the slightest disturbance, in tissues lying outside the swifter currents of the circulation.

Dr. Ralfe regards the action on some special nervecentre of 'the predisposing causes of gout' as a probable factor in the production of the gouty attack. Accumulation of uric acid in the blood, and deposition of urate of sodium in the tissues, are the *results* of the latter.

## PFEIFFER'S THEORY: THE GOUTY ATTACK DUE TO A RE-SOLUTION OF THE DEPOSITS.

Pfeiffer endeavours to explain gout and gravel on the assumption that in the 'uric acid diathesis' the acid takes on a less soluble form, is less freely excreted, and is more liable to be precipitated in a gradual and latent manner into the tissues. So long as nothing interferes with the insoluble state of the deposits, nothing will happen. Any wave of increased alkalinity passing over the blood would, however, bring on pain, and perhaps a gouty attack, which Pfeiffer explains by supposing that the deposits are then partly dissolved, and that the urates in solution occasion the local irritation. Thus, Pfeiffer assumes that during the arthritic attack the insoluble form of uric acid is reconverted into the soluble form. This theoretical view he supports by his clinical observation of increased pain after administration of alkalies, and of the relief to the pain afforded by acids, especially by salicylic acid in large doses.\*

The Excretion of Uric Acid as influenced by Age.—
Pfeiffer maintains that the relative amount of uric acid

\* Pfeiffer professes to have obviated the pain usually produced by subcutaneous uric acid injections by means of a previous course of 5 to 8 grammes of hydrochloric acid, or of phosphoric acid administered daily. As pointed out by Sir W. Roberts, it is extremely difficult to make much impression on the reaction of the blood, additional quantities of acid or alkalies being quickly expelled by the kidney. Freudberg (Virchow's 'Archiv,' Bd. 125, p. 566, quoted by Levison, loc. cit., p. 49) and others have established this fact by careful experiment. Thus, daily doses of 4 to 8 grammes of hydrochloric acid do not alter the reaction of the blood; it takes from 10 to 30 grammes of lactic acid to lessen the alkalinity of the blood by one-fifth to one-quarter; and 5 to 10 grammes of tartaric acid to reduce it by one-sixth. In the same way sodium bicarbonate in doses of 5 to 15 grammes, though they sometimes increase the alkalinity by one-fourth, at other times may make no difference whatever to the reaction.

normally excreted bears a definite relation to age, and that it progressively diminishes with increasing years. Pfeiffer gives the following amounts for 100 kilos of body-weight, during the successive decennia:

 First decennium
 ...
 ...
 1'280 grammes.

 Second decennium
 ...
 ...
 1'113 ",

 Third decennium
 ...
 ...
 1'024 ",

 Fourth decennium
 ...
 ...
 0'965 gramme.

 Fifth decennium
 ...
 ...
 0'882 ",

 Seventh decennium
 ...
 ...
 0'752 ",

 Ninth decennium
 ...
 ...
 0'577 ",

The Uric Acid Filter.—Pfeiffer has claimed for gouty urine the curious peculiarity that when filtered through o'5 gramme of pure uric acid it leaves its uric acid on the filter.\* The same is observed in the case of healthy urine, but much more uric acid (2 to 3 grammes) is said to be required to ensure the result. Pfeiffer regards this difference as a confirmation of his view that in the gouty diathesis the urates assume a less soluble modification than that which belongs to the physiological state; whilst during the gouty attack the insoluble variety passes again into the soluble form.

Pfeiffer's alleged insoluble modification of the urates in gout has been placed in the light of a superfluous assumption by Sir W. Roberts' investigations into the chemical factors influencing the decomposition of the quadriurates.

# EBSTEIN'S THEORY OF THE DESTRUCTIVE ACTION OF URATES ON TISSUES.

Ebstein attributes the uric acid excess in the blood, not to any pre-existing renal defect, though a primary gouty

\* Athough this method of testing for the presence of the 'gouty diathesis' has met with some support at the hands of Schetelig and Camerer, its value is called in question by Ebstein, Feliziani, and Sir W. Roberts. Sir W. Roberts finds that any urine may be cleared of its uric acid by repeated filtration through the uric acid filter.

nephritis beginning with uratic deposits and ending in fibrosis sometimes occurs, but to an abnormal extension of its source of supply. Bone-marrow, cartilage and other tissues are supposed to take on its manufacture. The resulting excess in the blood may be successfully dealt with by increased renal excretion, or even, perhaps, by chemical decompositions occurring in the blood;\* but events do not always take so favourable a turn.

Any accidental check to the free circulation of the impure blood will produce all the nervous discomfort and the various symptoms of the gouty state. Locally, if there should be actual arrest of the lymph-stream, the concentrated solution of urates contained in the stagnant lymph will exert its deleterious action, and may even induce in the tissues with which it is in contact necrobiotic changes. All may yet be well, however, if the circulation be set going again without too great a delay. In some such way may be explained the foci of beginning necrosis which Ebstein professes to have found in portions of the cartilages of gouty joints which were as yet free from any biurate crystals. In those portions where crystallization had occurred, a necrotic surface was invariably exposed, after dissolving the crystalline deposit, and this Ebstein attributes to the solution of urates acting as a chemical poison for the tissues.

As a result of the necrotic process, the tissues alter their alkaline reaction of its solution to an acid one. At that moment a precipitation of sodium biurate takes place: a fit of the gout has been started.

Ebstein's theory is open to many objections. The

<sup>\*</sup> In this connection may be mentioned the observation by Salomon (quoted by Levison, *loc. cit.*, p. 45), that he could detect uric acid in gouty blood only when quite fresh; after allowing it to stand twenty-four hours at a temperature of 37° C., all trace of it seemed to vanish.

fundamental proposition that in gout uric acid is produced in a variety of tissues not normally concerned in its manufacture is set aside by Horbaczewski's demonstration that in health uric acid is a by-product of the metabolism of almost all tissues.

With an over-production of uric acid and with healthy kidneys—conditions for which Ebstein contends—the urine should contain an excess of uric acid, instead of a diminished amount (Pfeiffer).

Ebstein's experiments in fowls and serpents cannot be made to apply to human pathology, not even those which resulted in a production of necrotic patches in the liver and in the heart-wall after ligature of both ureters in fowls; and it is also to be noted that in the kidney the necrotic process was obtainable only after subcutaneous injections of potassium chromate. As pointed out by Levison, experimental ligature or destruction of both kidneys must set up a uræmia rather than anything comparable to gout.

Lastly, the alleged strong toxic property of solutions of the urates has not been confirmed by other observers. Pfeiffer's experiments\* show that solutions of urates of a concentration such as may occur in the living body are quite unable when injected into the tissues to set up necrotic changes, though they may produce pains and irritation. Solutions of pure uric acid act as violent irritants, but they are not in question.

<sup>\*</sup> Quoted by Levison, loc. cit., p. 48.

#### CHAPTER VIII.

### THE MODIFIED CHEMICAL THEORIES.

THE THEORIES OF HEPATIC INADEQUACY—MURCHI-SON'S AND LATHAM'S VIEWS.

THE intimate connection existing between gout and hepatic derangement has been recognised by most pathologists, but it has received special attention at the hands of Murchison, and more recently of Professor Latham, and to their ideas a brief reference must be made.

Murchison, whose views on lithæmia in connection with various diseases are too well known to need comment, saw in gout, as in diabetes, a special variety of functional derangement of the liver; at the same time he admitted renal inadequacy, especially in the later stages of gout, and an accumulation of uric acid in the blood, as associated factors in the disease.

Murchison's pathological and clinical researches have gone far to confirm the experimental evidence supplied by Claude Bernard and subsequent physiologists in favour of the metabolism of the albuminous supplies within the liver, with the direct production of urea, and probably with uric acid as a by-product.

Professor Latham\* has elaborated a clinical theory which defines more closely the manner in which a failure

<sup>\*</sup> Cf. 'On the Formation of Uric Acid in Animals,' 1884, and Croonian Lectures on Rheumatism, Gout and Diabetes, 1886.

of the hepatic function may lead to an abnormal production of uric acid.

If the glycocine brought back to the liver by the portal vein, with other reabsorbed constituents of bile, instead of being transformed, as Professor Latham considers that it should be, into urea, should remain unaltered, whilst other bodies, such as leucine and tyrosine, undergo the normal conversion into urea, various combinations may eventually arise between the glycocine and the urea. soluble compound known as hydantoin being formed in this way and carried to the kidney, and combining with some of the urea constantly present in that organ, would be transformed into ammonium urate, which would be partly excreted and partly reabsorbed into the blood. The substitution of a molecule of the sodium abundantly contained in the serum for a molecule of ammonium would finally give rise to sodium biurate, and thus supply the material for the gouty deposit. Professor Latham's theory is in harmony with the fact that the absence of uric acid from the urine of herbivora coincides in them with the absence of glycocine from the bile.

The non-conversion of glycocine into urea, which would be the central fact in the production of gout, finds a parallel in diabetes, where glucose likewise fails to be further elaborated. Both conditions would have their explanation in a disturbance and a partial suspension of the normal metabolism of the liver.

In the case of gout, the partial paralysis of the hepatic function would be probably due to the excessive stimulus of food in the absence of sufficient exercise, and might be compared to the paralysis of the submaxillary gland brought about by atropine.

In addition to purely chemical irregularities connected with the liver, Professor Latham looks to the nervous system for the mechanism which brings about the attacks and the inherited liability to them, and also determines their localization. He ascribes a leading share in the pathogeny of the disease to the central nervous system, without specifying the locality of the suspected change. Whether it be situated in the medulla oblongata or in the spinal cord, it might be either acquired or inherited, and would explain in the individual the existence of a predisposition to gout.

Latham suggests that if the hepatic disturbance be assumed to have its determining cause in some nervous weakness of the medulla oblongata within the district of the origin of the vagus, the weakness might also explain the morbid reactions induced by an excess of uric acid in the blood within the area of distribution of that nerve, viz., the gastric, respiratory, and cardiac troubles so commonly observed in the gouty; whilst the affection of the same centre (if concerned in the trophic innervation of the joints), or of some other, perhaps spinal, centre presiding over the nutrition of articulations, might be an active determining factor of the local processes in the joints.

# DR. HAIG'S THEORY OF URIC ACID AND EXCESSIVE VASCULAR TENSION.

Dr. Haig's views stand alone in their originality and unhesitating boldness.

As in Garrod's theory, what may have preceded uric acid is not under discussion. Uric acid is made our starting-point and our beginning, and if we are not overanxious as to the stability of this mid-air foundation, everything is evolved smoothly from it on the lines of the theory. The central facts assumed by Haig are:

(1) That uric acid is toxic in the soluble form, in which

it circulates in the blood; and (2) that it is mechanically irritating when deposited in the joints.

The stress of the toxic effects falls largely on the vascular system and on the vaso-motor function; but the consequences are varied. The range of the deleterious effects is not even narrowed down to the gouty complex. All the possible results of peripheral vaso-constriction, and of heightened vascular tension, are capable of being referred to uric acid as a cause. The morbid results of an excess of uric acid thus constitute a considerable group, that of the 'uric acid diseases,' of which gout is merely one member.

Another original view is that taken of the pathology of rheumatism. Rheumatism is included in the 'uric acid diseases.'

'In place of rheumatism and gout I see but one disease, an arthritic irritation due to the presence of urates, which under some circumstances will be limited to one joint (gout), or affect several joints contemporaneously or in succession, and the heart also (rheumatism).'\*

Haig undertakes to produce an arthritis clinically indistinguishable from gout or rheumatism in one perfectly healthy. 'All that is necessary is to get a little uric acid into the blood, and when one can see from the slow pulse, scanty urine, and more or less headache and mental depression, that it is actually present there, one must administer, as quickly as possible, some acid or other drug which interferes with the solubility of uric acid and drives it out of the blood into the tissues.' Some working of the joint, or the application of some irritation, will also be necessary.

The normal proportion between the uric acid and the

<sup>\*</sup> Alexander Haig, M.D., F.R.C.P., 'Uric Acid as a Factor in the Causation of Disease,' etc. Second edition, 1894, p. 83.

urea excreted is assumed by Haig to be constant at 1-33 or 1-35, and its pathological variations are studied elaborately.

The quantity of uric acid in the blood\* varies much; except perhaps in pneumonia the blood always contains less than the liver or the spleen, which, of all the organs, contain most, the kidneys containing less, and the muscles least.

The joints are also recognised among the structures in which uric acid is stored. The shooting and pricking pains in the joints after a dose of acid are held by Haig to be due to the uric acid driven into them out of the blood.

Among the *local factors* of gout, Haig† refers to old joints as probably being less vascular and less alkaline than young joints, besides being more exposed to the influence of cold.‡

The arguments adduced in support of the toxic effects are singularly ingenious, but they do not include any attempt to explain the derivation of uric acid, otherwise than by ingestion; nor the mechanism of its operation in the production of gout; nor why the accumulations of uric acid from the habitual and great over-indulgence in animal food should, in many cases, remain absolutely unproductive of any tendency to gout.

The main source of uric acid is assumed to be the amount actually contained in the food, or that arising from its nitrogenous elements. An animal diet having for its consequences the accumulation of large quantities of uric acid, which, in the various situations in the body, Haig estimates at an aggregate store of some 350 to 400

<sup>\*</sup> Haig, loc. cit., p. 73. † Loc. cit., p. 313.

<sup>‡</sup> Discussion on salicylates and rheumatism. 'Proceedings of the Royal Medical and Chirurgical Society,' April, 1890, p. 109.

grains per annum, practical conclusions are drawn in favour of vegetarianism.

The behaviour of the ingested uric acid is described in the following words:

'Uric acid, when taken by the mouth, passes into the blood, and, when the conditions in that fluid are favourable to its solubility, remains there till it is excreted in the urine; that it is not to any appreciable extent converted (as was supposed) into urea; that the rise of urea which these substances produce is secondary to the rise of acidity, which they also produce; and that other acids which introduce no nitrogen into the body produce similar rise in the excretion of urea.'

Any causes, such as dyspepsia, producing a fall in the acidity, will produce uricacidæmia. When digestion improves, acidity occurs, and drives the uric acid into the joints.

It is to be noted that the gouty attack occurs at night, during the acid tide.

In the blood,\* according to Haig and others, excess of uric acid occurs in connection with deficient oxidation. He refers to Dr. E. Peiper's observation that the alkalinity of the blood is diminished in all fevers, except when these are complicated with dyspnæa or cyanosis. This view is practically equivalent to that of Haig, who follows up the causation of the excess, beyond a deficient oxidation, to a consequent deficient formation of acid.

Perhaps the most striking feature of originality is that those metabolic irregularities in which others have looked for the source and origin of uric acid are attributed by Haig to the action of uric acid itself. As an instance of the influence of uric acid on the general metabolism, Haig† points out that an excess of uric acid in the blood pro-

<sup>\*</sup> Haig, loc. cit., p. 60.

duces a diminution of the capillary circulation, and therefore a general slackening of metabolism, and a lessened formation of urea, and of acids and acid salts which usually keep pace with urea. The increasing alkalinity of the blood induces more and more marked uricacidæmia. But if a drug be given which clears the blood of uric acid, the process may be quickly and completely reversed: 'up goes the formation of urea and of acids, a steady and progressive upward metabolism is started, and the blood is kept clear of uric acid.' This is the answer to the question: Why does a very minute dose of a nitrate, a few grains of a sulphate, or a small portion of a grain of calomel, relax the arterioles all over the body, and cure headache or mental depression?

During the early days of a fever\* metabolism, being very active, diminishes the alkalinity of the blood; uric acid being removed from the blood, pains are apt to be felt in the joints and elsewhere; but later on metabolism languishes, alkalinity of the blood rises, and with the return of uric acid, pulse tension is apt to rise, and, as a fact, dicrotism towards the termination of the fever may cease to be observed.

Fever lessens the sugar passed by diabetic patients, because, the blood being cleared of uric acid, the arterioles are relaxed and metabolism is quickened.

The effect of a surgical operation to not the metabolism is practically the same as that of a fever. The case of a woman is adduced who was under observation for one or two days before, and one or two after, abdominal section. After the operation the amount of urea rose to two or three times the normal amount. This Dr. Haig regarded as the result of the very active metabolism locally induced by the operation, the patient being placed on a highly

nitrogenous diet at the expense of her tissues. The acidity rising with urea, it was thus argued that the surgical operation had the effect of clearing the urates out of the blood, of relaxing the arterioles, and of further increasing the metabolism.\*

Haig disbelieves in inherited weakness, innate delicacy, or transmitted neurosis, in connection with uric acid diseases, and regards as the chief factors in their causation improper food, impure blood, and consequent increased

\* In the paroxysmal form of anamia Haig points to an increased coagulability of the blood, and refers it to uric acid (loc. cit., p. 254).

Oxalate of lime is present in the urine in that disease. Dr. Brunton has reminded us (*Brit. Med. Journ.*, vol. i., 1885, p. 167) that concentrated urates in presence of sulphuretted hydrogen generate oxalic acid. The sulphuretted hydrogen probably is supplied from cabbage, and similar vegetables rich in sulphur, in the intestinal canal.

The excessive intestinal putrefaction noted in epilepsy by Herter and Smith (New York Med. Journ., August and September, 1892) is explained in the same way as in the paroxysmal and in the pernicious forms of anæmia, being produced by uricacidæmia, general arteriolar contraction, excess of uric acid, and therefore some destruction of blood, whilst the contracted arterioles suspend gastro-intestinal digestion (cf. Dr. A. E. Garrod, 'Royal Medical and Chirurgical Society's Transactions,' vol. lxxv.: 'The Anæmia of Rheumatism,' etc.).

Haig (loc. cit., p. 249) also draws attention to the active metabolism of young girls at the age of thirteen; they about that time increase by some 10 to 11 lb. in weight in the course of a year (at seventeen or eighteen the increase is only about 2 lb.). The result of this activity is considerable acidity of the urine and low alkalinity of the blood, leading to a storage of uric acid in the body, in the liver, spleen, and probably other fibrous tissues.

The latter is further increased, doubtless, where there exists a tendency to rheumatism. At a later period, as nutrition falls, alkalinity rises, uricacidæmia supervenes, with contracted arterioles, slow tense pulse, headache, etc.

Menstruation still further lowers metabolism, and tends to upset the digestion.

'Stimulation breeds stimulation; for if we clear the blood of uric acid for a few hours, metabolism will go ahead, and keep the blood clear.'

blood-pressure. One factor may, however, be inherited, viz., 'a slight variation in the size and distribution of the arteries at the base of the brain, rendering the intracranial circulation especially liable to be affected by unduly high blood-pressure.'

In conclusion, gout, according to Dr. Haig, would be in the strictest sense a 'uric acid disease,' its local phenomena being merely the result of a deposition of urates into the joints, and its constitutional phenomena being among the many results which he traces to their excess in the juices.

### CHAPTER IX.

# THE HISTOGENOUS THEORIES, OR THEORIES OF A PRIMARY PRE-URATIC TISSUE CHANGE.

The Nature of the Localizing Influence. — Long before Scudamore, Van Swieten had called attention to the special liability of the foot to various accidental lesions which may act as localizing factors. Sir A. Garrod\* himself dwells on the influence of local mischief in causing gout to appear in the injured parts. Many others have also thought and spoken of the link which must exist between the structural and the chemical pathology of gout, though none have succeeded in explaining wherein it consists. It was obvious from the first that the uric acid theory was itself in need of further explanation. Among recent theories none therefore deserve greater attention than those which seek to define strictly the connection between tissues and juices and their mutual behaviour.

Gairdner had expressed the view that the changes in the urine and the increase in uric acid in the blood described by Garrod were rather a consequence of gout than its cause, and had suggested the probable existence of some preliminary nervous factor. The same agency had also been admitted by Laycock, who taught that gout is not of necessity always articular, or even always combined with joint trouble; but a more definite advance towards the elucidation of the uric acid problem, which has culminated in late researches and discoveries, was foreshadowed in his suggestion that a production of uric acid in the tissues rather than in the blood was characteristic of gout. The same idea was subsequently expressed, though still in a general way, by Parkes and by Barclay.

# THEORIES OF PARKES AND OF BARCLAY—A PRIMARY ALTERATION IN THE METABOLISM OF THE BLOOD, OR OF THE TISSUES.

Parkes,\* whilst disinclined to admit a primary inadequacy of the kidney, believed nevertheless that uric acid was not only produced in excess, but unduly delayed in the system. Holding the kidney responsible for the retention of uric acid, he identified the retarding influence with 'important antecedent aberrations in metamorphosis in the blood or in the tissues, the abnormal products of which might be capable of holding back uric acid and other substances, such as phosphoric acid.'

Barclay† recognised the check to the renal elimination of uric acid described by Sir A. Garrod. The kidney at this stage was not, however, to be considered a perfectly healthy organ, but as suffering together with other organs under the influence of a primary change in the blood corpuscles, directly due to the continuance of a faulty diet, till cell after cell became affected and the gouty state induced. The retention of uric acid was to be regarded 'as a symptom, a consequence of the attack of gout, and not as its cause.' The efficacy of colchicum, and the

<sup>\*</sup> Parkes, 'On Urine,' p. 298; London, 1860.

<sup>†</sup> Barclay, 'On Gout and Rheumation in Relation to Disease of the Heart;' London, 1866.

relative failure of alkalies, were for Barclay arguments in favour of this theory.

Barclay's selection of the red-blood cell as likely to be specially concerned in the evolution of gout possesses interest in connection with more recent theories which throw analogous suspicions on the leucocyte. His views and those of Parkes were important steps towards the fundamental principle subsequently enunciated by Ord and, at a later date, by Ebstein, that the tissues take an active share in determining the deposition of uric acid.

## THEORIES OF ORD AND OF EBSTEIN—ANTECEDENT STRUCTURAL CHANGES CONNECTED WITH THE CHEMICAL CHANGES.

Dr. Ord's\* theory is comprehensive, and recognises the part played by the nervous system, as well as that which belongs to the tissues. He seeks the cause of the primary deposition of uric acid in some essential defect, inherited or acquired, in the fibroid tissues. From this original deposit an overflow takes place into the blood, ultimately leading to the invasion of the cartilages and of other tissues. Dr. Ord also believes in the influence of nervous reflexes in causing a propagation of the morbid process to distant parts. Not only is this extension promoted in a reflex way, but a transference of the disease to distant sites by direct nervous agency is traced in the mode of production of the acute attacks.

Gout may be regarded as a disease of degenerations, both general and local. The local tissue degeneracies supply a basis for the uratic deposits, and the general degenerative changes multiply the sites exposed to an infiltration from the contaminated blood; whilst reflex mechanisms

<sup>\* &#</sup>x27;St. Thomas's Hospital Reports,' New Series, vol. iii., p. 237, 1872; and Medical Times and Gazette, vol. i., p. 233; 1874.

step in as additional determining agents. It is further pointed out that the local acute inflammation is not of necessity specific in every instance, *i.e.*, due to the irritation of the degenerating tissues by the crystalline deposits, but that it may be set up at times by other exciting causes.

Dr. Ord's conclusions are these:

- I. Gout is a mode of decay of the whole system, marked by the deposit of urate of soda in and about joints, and by local inflammation of a particular kind.
- 2. The deposit of the urate is a result of local or general disintegration, and is not to be regarded as a means of eliminating waste from the blood.
- 3. The local inflammations do not necessarily depend upon the deposit of urate, and the deposit is not a consequence of inflammation; at the same time, it is probable that excess of urate in the blood produces irritation of tissues.
- 4. The local inflammation is peculiar in respect of the ease with which it is produced, of the pain by which it is attended, and of the products, which are chemical rather than structural; chemical substances of low molecule, tending to crystallize or to be dissolved, being formed in the part, instead of substances of high molecule tending to be organized. Interstitial subcrystalline deposit is common, suppuration rare, in gout.
- 5. The local inflammations are set going by local exciting causes.
- 6. The local degenerations and inflammations tend to infect the rest of the system through the blood, and to set up similar reactions elsewhere through reflex nerve action.

W. Ebstein\* also admits that gout is based upon local

<sup>\*</sup> Ebstein, 'Die Natur und Behandlung der Gicht;' Wiesbaden, 1882.

degenerative changes, but he regards them as produced by a destructive action of the concentrated solution of uric acid contained in the juices. The prime factor is the faulty metabolism, induced in some unexplained way in the muscles and in the marrow of gouty persons. Impregnation with soluble neutral urate and toxic degeneration and necrosis are the early changes occurring in those parts which subsequently suffer infiltration with the crystals of sodium biurate, crystallization being itself brought about by the acidity of the necrotic tissue. The reactions of surrounding parts to this necrotic and irritative process constitute gouty inflammation. Crystallization of the deposit is thus a secondary event, occasioned by the conversion of the neutral into the acid urate under the influence of an acid which he supposes to be generated in the necrotic areas.\*

Ebstein has endeavoured to prove by intracorneal injections of a saturated solution of uric acid in 5 per cent. sodium phosphate solution that irritating properties belong to uric acid and its compounds. Sir W. Roberts points out that the abundant and voluminous gelatinous urate which would soon separate from the solution in question would not fail to irritate the cornea, owing to the extent of the obstruction it would occasion. The comparative intracorneal injections with pulverized uric acid and with magnesia suspended in water are also misleading, owing to the opposite behaviour of the two substances in contact with the alkaline juices of the cornea.

\* The observations of Sir A. Garrod, of Cornil, of Ranvier, of Sir Dyce Duckworth, and of others, show that necrosis is not a necessary preliminary. The needles of crystalline urate will, according to Sir Dyce Duckworth, push their way without any respect for the component elements of the tissue, as if it were an indifferent or homogeneous medium; and it is more natural to regard the destructive changes as secondary to the pressure effects and inflammation due to the deposit.

Professor Ebstein also studied the deposition of urates in fowls after ligature of the ureters, or after progressive abolition of the renal function by *injections of chromate of potassium*. Sir W. Roberts has shown that in them the biurate is precipitated in the tissues in the gelatinous form, whereas in mammals the concentration is never sufficient to allow the gelatinous, but only the crystalline variety to be precipitated.

That the case of fowls and that of man are not comparable is further illustrated by the fact that Ebstein describes deposits in the liver and muscles in fowls, situations in which they do not occur in human gout.

In conclusion, Ebstein does not identify the uric acid as a direct local decomposition product of the tissues. The share of the latter in the process is limited to the faulty metabolism of muscles and marrow which supplies the excess of uric acid, and to the local precipitation of the biurate through the acidity due to the local necrosis. The theory of the direct histogenous derivation of uric acid, formerly hinted at by Laycock and by Parkes, and taught more definitely by Ord, did not reach maturity until Professor Latham worked out a chemical explanation of the process, and Horbaczewski demonstrated the steps in the transformation of nuclein into uric acid.

### CHAPTER X.

### THE 'NERVOUS' THEORIES OF GOUT.

THE middle of the last century witnessed a reaction against the humoral theory which had long prevailed, and a revival of solidism. Stahl's great work\* is regarded as the starting-point of the modern speculation as to the nervous origin of gout.

Following this lead, Cullen† threw the weight of his clinical experience and authority into the scale. Gout was considered by him to be a disease primarily of the nervous system.

Again, at a much later date, in 1847, Henle took up the same idea, and taught that 'the origin of the affection was probably to be found in the central nervous system.'

Professor Gairdner,‡ whose philosophical work appeared soon after the publication of Garrod's theory of renal inadequacy, endeavoured to trace the defective elimination of uric acid as a result of some more distant cause, and found suggestive analogies in the check to the renal function induced by shock, emotion, and hysteria. Pro-

<sup>\* &#</sup>x27;Theoria Medica Vera,' etc.; G. E. Stahl (Halle, 1737): 'De Doloribus Spasticis Arth<sup>co.</sup> Podagricis,' § xxxviii., p. 1040 (quoted by Duckworth).

<sup>†</sup> First lines of the 'Practice of Physic,' 1784: vol. ii., part i., chap. xiv.

<sup>‡ &#</sup>x27;On Gout: its History, its Causes, and its Cure,' by William Gairdner, M.D.; London: J. Churchill, 1849.

fessor Gairdner may thus claim to have been in effect, without at the time explicitly asserting that position, one of the earliest supporters of the modified nervous, or neuro-humoral theory of gout, or, at any rate, of the view that the nervous system is implicated in the pathological events.

Various other observers, recognising the directive influence exercised on other tissues by the nervous system, took up a similar position. Laycock was a strong believer in the influence of altered innervation.

The nervous theory of gout has another prominent advocate in Dr. Edward Liveing,\* who sees in its paroxysmal, periodic, and other features reason to suspect a nervous origin of the disease.

Within recent years a fresh impulse has been given in the same direction by Dr. Ord's observations of a nervous factor in some affections of the joints; by Dr. Buzzard's suggestion of a centre for the nutrition of joints, which he would localize in the region of the fourth ventricle rather than, as Charcot had been led to think by the frequent association of tabetic joint trouble with gastric crises, in the anterior cornua of the spinal cord; and by Professor Latham's assumption of some central affection of the nervous system, by which he seeks to explain the altered hepatic metabolism which he regards as the immediate cause of the gouty trouble.

### DUCKWORTH'S THEORY—GOUT AS A TROPHO-NEUROSIS.

The latest exponent of the nervous theory, Sir Dyce Duckworth,† had claimed as far back as 1880‡ a neurotic

<sup>\* &#</sup>x27;On Megrim, Sick-Headache and some Allied Disorders,' p. 404; London, 1873.

<sup>† &#</sup>x27;A Treatise on Gout;' London, 1889. ‡ Brain, April, 1880.

origin for gout. He describes gout as 'a primary neurosis,' 'a functional disorder of a definite tract of the nervous system.' 'In primary or inherited gout the toxæmia is dependent on the gouty diathesis. In secondary or acquired gout it is directly induced by such habits as overload the digestive and excretory organs, and constantly prevent complete secondary disposal of the nutritional elements of food. If then, together with such toxæmia, distinctly depressing and exhausting agencies, affecting the nervous system, come into operation, the special neurotic manifestations of the gouty diathesis will occur, and be impressed more or less deeply upon the individual and his offspring.' By neurosis he understands 'a peculiar disposition or tendency on the part of the nervous system, or some definite tract of it, towards morbid evolution or manifestation of nerve functions.'

'A most marked feature in all neurotic affections is the paroxysmal tendency.' Other features, all of which are traceable in gout, are periodicity, instability, and alternations in their manifestations, and a liability to be excited or aggravated by undue nerve strain and by depression. In all these respects a likeness may be traced between gout and a typical neurosis.

Whilst the neurosis is the nervous agency in the gouty attack, the gouty habit is the outcome of a neuro-trophic defect.

Entering into further detail, and assuming with Ebstein 'an undue formation of uric acid in unusual localities,'\* and with Beneke, Bouchard, and Rendu, 'a primordial vice of nutrition,' 'a peculiar incapacity for normal elaboration of food within the whole body, whereby uric acid is formed at times in excess, or is incapable of being duly transformed into more soluble and less noxious pro-

<sup>\*</sup> E.g., bone and muscle.

ducts,' Sir Dyce Duckworth ascribes this disability to disturbed innervation, and to 'perverted neuro-trophic functions,' i.e., to a tropho-neurosis.

From this description, it will be readily gathered that the nervous theories entertained by some modern pathologists, and in particular by Sir Dyce Duckworth, are of a mitigated type; they are considerably toned down from the uncompromising type originated by Cullen. A humoral aspect of gout is freely admitted by all, and the humoral changes are freely discussed. Thus, Sir Dyce Duckworth expressly states, 'I cannot dissever the two ideas, and hence I affirm that gout is a neuro-humoral disease.' Still, he looks beyond the chemical pathogeny of gout for 'a presiding nervous element,' and he finds it in the neurosis, which may be either 'implanted,' that is, primarily impressed as an individual heritable feature, or 'secondarily induced, owing to some toxemic condition.'

On the other hand, the toxæmia itself reacts on the nervous system in a secondary fashion, aggravating the natural tendency. In the same way, in acquired gout also, the nervous system gradually falls under the influence of that weakness, which, though not itself a neurosis, ends in producing the gouty neurosis, and in being capable of hereditary transmission.

This inherited predisposition to the gouty trophoneurosis is part of a still wider peculiarity of the individuum recognised by Sir Dyce Duckworth as the arthritic diathesis, or arthritism, and consisting in a special vulnerability of the 'joints and other structurally allied tissues, and in their special liability to trophic changes,' associated with a marked sensitiveness to changes of temperature, soil, and climate. He regards arthritism (which was originally defined by Pidoux, and subsequently adopted by Charcot and recognised also by Hutchinson)

as 'a diathetic habit of body, from which arise, as branches, two main and distinct classes of disorder, commonly recognised as gout and rheumatism.'

As regards the chemical changes in the blood and the structural changes in the articulations, the theory under review is in complete agreement with the views propounded by modern pathology, which are described under another heading.

It was necessary to enter into a detailed consideration of the nervous section of this working hypothesis, because it represents the most complete theory published in this country on the general pathology of gout, and because the able advocacy of its propounder has given it the support of arguments derived from pathological analogy and from clinical inference, which will demand careful examination and searching criticism before they can be either disproved or adopted.

### WADE'S NEURAL THEORY OF GOUT.

The latest addition to the nervous theories of gout is Sir Willoughby Wade's important 'neural theory.' Its exposition, involving a detailed account of original clinical observations, will be more profitably undertaken in the Clinical Section, to which the reader is referred. Gout, according to the neural theory, is not a mere neurosis, but largely partakes of the characters of a neuritis.

Taking into account the shortness of the acute attack, at any rate as regards the pain, it will probably be asked whether the changes special to neuritis would have time to evolve and to disappear within so brief a period. This and other criticisms must, however, be deferred till the theory itself has been more fully set forth.

### III.

# THE CHEMISTRY OF GOUT.

### CHAPTER XI.

# SIR WILLIAM ROBERTS' INVESTIGATIONS ON THE PHYSIOLOGICAL AND PATHOLOGICAL CHEMISTRY OF URIC ACID.

### URIC ACID IN THE BLOOD.

The percentage of uric acid in the blood in health is very small. At any rate, the thread experiment does not succeed in showing its presence in most cases. During the attack of gout the amount can be easily estimated. Sir A. Garrod found in a patient so high a percentage as I in 5,714; and Sir W. Roberts adopts the proportion of I in 6,000 as representing the state of saturation. By saturation he understands a percentage such that any addition to it will lead to supersaturation and to deposition of uric acid from the blood. According to him, supersaturation may be said to exist when lymph or synovia contains I in 6,000, and under-saturation when they contain less than I in I0,000 of the biurates.

The serum, or, rather, the plasma, is regarded by both authorities as being the carrier of the uric acid.

Sir W. Roberts' experiments were conducted with serum, but to a large extent also with artificial serum. He

made the important observation that by adding to water sodium chloride or sodium bicarbonate in the proportion in which they are contained in serum (neglecting the small proportion of sodium phosphate, which was found experimentally not to exert any effect on the solubility of the urates), a standard solvent could be prepared\* which in experiments reacted in the same manner, with uric acid and urates, as blood serum, traces only of sodium biurate being dissolved by it at 100° Fahr.

The chemical state in which the uric acid is held in the blood was originally assumed to be that of a urate. Sir W. Roberts has endeavoured to trace the chemical changes undergone by the acid during the passage from the healthy to the gouty state. But a preliminary acquaintance with his description of the normal chemistry of uric acid is essential.

# THE SALTS OF URIC ACID: THEIR CHANGES AND THEIR BEHAVIOUR.

Uric Acid, the Biurate and the Quadriurate. — Sodium biurate† has been proved by Sir W. Roberts to be peculiar to gout, never existing in the human body except as a by-product of the disease.

The form in which the salts of uric acid are circulated, secreted, and excreted, is that of the quadriurate, in which a double molecule of uric acid is associated with a single molecule of a monovalent base. Prior to Sir W. Roberts'

# \* Composition of the standard solvent:

Sodium chloride... ... o'5 gram.
Sodium bicarbonate ... ... o'2 ,,
Distilled water ... ... ... 100 c.c.

† The neutral or dimetallic urate is, according to Sir W. Roberts, merely a laboratory product, and never occurs in the normal economy.

researches, this compound had been described by Bence Jones,\* but his discovery had been forgotten.

The chemical formula

H<sub>2</sub>(C<sub>5</sub>H<sub>2</sub>N<sub>4</sub>O<sub>3</sub>), MH(C<sub>5</sub>H<sub>2</sub>N<sub>4</sub>O<sub>3</sub>)

or

H<sub>2</sub>Ū, MHŪ.

suggests that the two uric molecules are conjugated rather than combined. So slight an influence as that of a bulk of water suffices to separate them, and to cause uric acid to crystallize. The molecule of metal in the remainder now becomes the centre of a fresh quadriurate group, which in its turn will be split up; and the process will repeat itself till all the uric acid has been deposited. This reaction is, therefore, a means of estimating the amount of uric acid present in a solution.

Uric Acid as a Urinary Sediment.—The appearance of uric acid crystals in urine after it has stood is shown by Sir W. Roberts to be due to the process described, slightly modified by the presence of sodium and potassium phosphates, which assist, nay, compel, the reconversion of the separated molecule of biurate into quadriurate, thus,

$$2MH\bar{U} + MH_2Po_4 = (H_2\bar{U}, MH\bar{U}) + M_2HPo_4,$$

whilst they themselves pass into the alkaline phase. This change, which explains the inability of the urine to hold uric acid as a biurate, occurs in all urines eventually; but the constituents of any particular urine exercise an influence on the time at which the reaction takes place.

- I. A high percentage of uric acid greatly predisposes to precipitation.
- 2. The alkaline reaction prevents precipitation.

<sup>\* &#</sup>x27;On the Composition of the Amorphous Deposit of Urates in Healthy Urine,' by Henry Bence Jones, Journal of the Chem. Soc., 1862, vol. xv., p. 201.

3. Much acidity greatly favours it; hence the addition of even small amounts of the alkaline carbonates

will delay the precipitation.

4. The great affinity of uric acid for the soluble urinary pigment probably tends to keep it in solution. At any rate, earlier precipitation occurs in urines which are deficient in pigment.

5. Deficiency in salines, and particularly in common salt, has also been shown by Sir W. Roberts to

be an accelerating influence.

These observations have an important bearing upon the pathology and treatment of calculus and gravel, to which further reference will be made.

The Gelatinous Quadriurate.—The quadriurate possesses greater solubility than either uric acid or the biurate. Moreover, its solubility varies greatly with temperature. By very rapidly cooling the solution of an artificially prepared quadriurate, Sir W. Roberts was able to obtain this body in a gelatinous form. It is in this amorphous variety that the quadriurate is, according to Sir W. Roberts, circulated through the economy in health, and excreted at the kidney.

The Gelatinous or Amorphous Biurate.—Greater pathological interest attaches, however, to the gelatinous or hydrated modification of the biurate. According to Sir W. Roberts' observations, the biurate liberated in the fashion described above from solutions of the quadriurates by addition of water is set free originally in a gelatinous form, and can be abundantly obtained by saturation with chloride of sodium crystals in the shape of spheres analogous to the spheres found in the urine of birds and serpents, which is presumably excreted in the gelatinous form.

The gelatinous deposit previously obtained by Dr. Ord\*

<sup>\* &#</sup>x27;On the Influence of Colloids upon Crystalline Form and Cohesion,' by W. M. Ord, M.D., etc.; London, 1879, pp. 72 and 219.

on cooling the mixture of a hot saturated solution of the ammonium or of the sodium urate with strong solution of an alkaline chloride or phosphate, and regarded by him as a true colloid, analogous to the colloidal form of silica, is considered by Sir W. Roberts to be rather an instance of hydration of a salt, for he was able to pass the combination unchanged through the dialyser.

Proceeding to a further study of this spurious colloid, Sir W. Roberts discovered that it represented a more soluble form of the biurate, and that it is probably formed when sodium biurate is dissolved in boiling water. Although ten times as much of the salt is then taken up as by cold water, no precipitate occurs on cooling until several days have elapsed, and this suggests a change in the molecular state of the compound. In truth, the biurate is readily precipitated in the gelatinous form from the cooled filtrate on saturation with the chloride, phosphate, or acetate of the fixed or of volatile alkalies in bulk, or in concentrated solution, or by means of a 20 per cent. solution of common salt; and it is then freely soluble in blood serum at 100° Fahr., or with the standard solvent (which hardly dissolves any of the crystalline biurate). Eventually the gelatinous precipitate (whether in the solid form or in solution) spontaneously suffers dehydration, and is reconverted into the crystalline variety, as originally discovered by Dr. Ord.

The Serial Changes undergone by the Uric Group, or the 'Maturation' of the Crystalline Biurate.—Sir W. Roberts shows that the quadriurate undergoes in the blood, lymph, and synovia changes exactly converse to those described above in the urine, and leading to the deposition of sodium biurate in the tissues. He has satisfied himself that 'uric acid is normally taken up, circulated, and voided as a quadriurate.' But when unduly accumulated and detained through renal inadequacy, as in the gouty state, in contact

with the sodium bicarbonate of the blood, it is partly transformed, with assumption of an additional atom of base, into the *biurate*, which is at first gelatinous, but, ultimately becoming dehydrated, is then ready to be precipitated, as this occurs in gout, in the crystalline state. This process is referred to as the 'maturation' of the biurate.

According to these views, the gouty process, so far as it relates to uratic sedimentation, might be explained on the basis of the varying degrees of solubility of the compounds of uric acid in the several media; it would be a matter of undersaturation and of supersaturation. The conditions affecting the solubility of the biurates in the juices, and particularly in the blood, the lymph, and the synovia, thus acquire special importance.

The solubility of the sodium biurate (pure, artificially prepared) in water was found to be about I in 1000 (at 100° Fahr.); in serum it was about I in 10,000, and in synovia similar results were obtained.

The great difference in the solvent power of the two fluids is illustrated by Sir W. Roberts' experiment. Two gouty incrusted metatarsal bones were respectively kept immersed in 6 oz. of blood and in 6 oz. of pig's serum, at blood-heat. The uratic deposit in the latter case was not completely dissolved until fifteen months—although the serum was three times renewed—whereas four days sufficed when water was used.

Saline solutions of varying strength, namely, the bicarbonate, the chloride, the sulphate, the phosphate, and the acetate of sodium, the bicarbonate, chloride and sulphate of potassium, the chloride of ammonium, and the chloride and the sulphate of calcium and of magnesium, were tested as to their behaviour as solvents of uric acid, with unexpected and remarkable results.

- 1. A general observation is applicable to all these salts; 'alkalinity or neutrality of the medium has not the slightest influence on the result.'
- 2. The salts of sodium strongly and uniformly (namely, in proportion to the sodium which they contained) diminished the solvent power, for sodium biurate, of the medium to which they were added, a maximum effect, to which greater concentration added little, being produced, in the case of the chloride and of the bicarbonate, by solutions containing o'5 per cent.
- 3. The salts of potassium were found to be absolutely inert as regards any influence on the solubility of the sodium biurate. Their solutions, of whatever strength up to a strength of o 5 or of I per cent., take up precisely as much of the biurate as does distilled water.
- 4. The salts of calcium resemble, but do not equal, those of sodium in their checking action on the solubility of the biurate of sodium.
- 5. The salts of magnesium act likewise in an adverse direction, although the effect is a much slighter one, and assimilates them more closely to the potassium group.
- 6. The salts of ammonium occupy an intermediate position between the calcium and the magnesium groups.

We now pass to the process of maturation, which has been stated to comprise: (1) a conversion of the original quadriurate into the hydrated biurate; (2) the dehydration of the latter into the crystalline biurate; (3) the precipitation of the anhydrous salt. It was experimentally shown by Sir W. Roberts that maturation is hastened by warmth, and that cold does not, as might have been assumed, accelerate the act of precipitation.

The Influence of Various Salines on the Progress of Maturation.—The influence of saline solutions studied in an

extensive series of observations (with the microscope as well as with the naked eye) gave the following results:

- Sodium salts (whether of alkaline or of neutral reaction) hastened considerably the precipitation within the maturating medium.
- 2. The salts of potassium 'sensibly retarded precipitation, but did not appreciably diminish the eventual amount of it.'\*
- Colchicum and magnesium salts appeared to delay precipitation, but their action in this respect was quite insignificant, or even doubtful.'
- 4. 'The salts of lithium had not the slightest influence either way.'
- 5. 'Piperazine and its chloride exercised no influence on the advent of precipitation.'

The Influence of Concentration.—By far the most important accelerating influence is a high proportion of uric acid. According to the amount present, he describes two forms of precipitation, which he assumes to have their counterpart in the joints:

- A copious and sudden precipitation (impregnation with uric acid I in 2,500).
- 2. A slow and scanty precipitation (impregnation with uric acid I in 5,000).†

In the latter case, the needles are extremely thin and short (one, two, or three times the diameter of a red cell), and are held to be probably incapable of setting up acute inflammation, though perhaps capable when occurring in the blood, or tissues, of producing the clotting of phlebitis or the symptoms of larval or irregular gout.

\* In the case of the potassium as well as of the sodium salts, the results were solely governed by the nature and quantity of the basic, to the exclusion of any influence from the acidulous radical.

† 1 in 5,714 was the proportion found in a gouty patient by Sir A. Garrod.

Thus the originally solvent action of blood serum or of the standard solution is followed, when opportunity is given for the gradual incorporation of more metal, by the formation of a biurate which eventually crystallizes in needles. By treating, according to this method, blood serum from the horse with an excess of uric acid, Sir W. Roberts was able to obtain a close imitation of the events in a 'fit of the gout'-'firstly, an impregnation of the medium with sodium quadriurate; secondly, a period of incubation or maturation, during which the quadriurate passes into biurate; thirdly, somewhat sudden precipitations of sodium biurate in the crystalline form; and lastly, restoration of the medium to comparative purity;' for at the end of the experiment on the fourth day, the supernatant serum in the corked phial was found to be comparatively free from uric acid.

### CHAPTER XII.

# THE CHEMICAL FACTORS APPLIED TO THE EXPLANATION OF GOUT.

### 1. THE LOCAL PRECIPITATION OF THE BIURATE.

THE Chemical Factors influencing the Uratic Precipitation.—
The chemical factors pointed out in the preceding study as favouring uratic deposition being excess of urates and excess of sodium salts, the importance of the differences between the various fluids and tissues of the body as to their richness in sodium salts, which are shown in the following table collated by Sir W. Roberts, will be manifest:

#### PERCENTAGE OF SODIUM SALTS.

	Per cent.				Per cent.	
Blood serum			0.40	Blood corpuscles		0'20
Lymph			0.70*	Brain		0.50
Synovia			0.80	Muscle		0.08
Cartilage			0.00	Spleen		0.04
Fibrous tissue			0.70	Liver		0'02

Among the tissues, brain and muscle seem predestined to escape, and cartilage and fibrous tissue to incur, the uratic infiltration—an arrangement of a distinctly conservative tendency. Among the fluids, synovia has the highest percentage of sodium. Its special proneness to

<sup>\*</sup> Or o'80, Munk and Rosenstein (Maly's Jahresbericht, Bd. xx., p. 40).

become the seat of uratic precipitation was demonstrated in Sir W. Roberts' 'maturation' experiments.

When synovia (the relatively thinner synovia from the hip-joint of the ox) was used, the same changes occurred as in the case of blood-serum; but the precipitation of the biurate began distinctly earlier, a circumstance correlated with the larger amount of salts contained in synovia.

A post-mortem infiltration of the upper layer of the cartilage was induced in the tarsal bones of a pig by suspending them at the ordinary temperature in a previously boiled, saturated solution of sodium biurate, which suffered precipitation in two or three days.

Moreover, the same conclusion is supported by observation in the human subject. Crystals of sodium biurate have often been found in synovial fluid; and it is for Sir W. Roberts matter of demonstration that the deposition proceeds from the synovial fluid, and does not originate in the cartilage, but is equivalent to a passive infiltration, and therefore more common and abundant at those points (at the periphery of the cartilages) where the synovia is in more constant contact.

Sir W. Roberts infers that deposits within the fibrous and tendinous structures are likewise passively induced from the synovia, and do not depend upon any primary local morbid changes in the tissues.

The Influence of Tissues and of Locality.—The connective tissues, which are almost exclusively\* those liable to gouty deposit, do not suffer equally in all situations. Those which enter into the formation of joints and are bathed in synovia are much more exposed, and among the joints the more superficial, and those least protected against the influence of cold, suffer most.

<sup>\*</sup> The muscular tissue, and the substance of the brain, liver, spleen and lung are conspicuously exempt. The kidney suffers.

A combination of these factors, with a general excess of uric acid in the system, would act in the most potent way, as, for instance, when general saturation of the blood happened to coincide with a local excess of sodium salts; that locality would then become the seat of the uratic deposit.

Sir W. Roberts throws out the further important suggestion that in proportion as the fluids in the several joints differ in concentrations, so also will the joints differ in their liability to uratic concretions.

The assumption, made by Sir A. Garrod and others, of a special attraction for uric acid in the joints, is at present beyond the range of proof. On the other hand, definite mechanical factors are suggested by Sir W. Roberts in explanation of the facts, viz., (I) the relatively motionless condition of the synovia; (2) the concentration of the synovial fluid, varying in different joints, and varying also in any one joint at different times, not only (as originally pointed out by Frerichs) under the influence of rest and of work—the latter leading to a smaller bulk and a greater concentration—but perhaps also, as ingeniously imagined by Sir W. Roberts, owing to general dehydrating influences, such as that of a heavy meal accompanied with copious libations of undiluted wine, or conceivably to some local dehydration, such as may be among the immediate effects of an injury to a joint; (3) the large proportion of mineral salts (almost exclusively those of sodium) special to synovia.

The Influence of General Excess of Uric Acid.—In explanation of the systemic factor essential to a precipitation of uric acid, viz., its accumulation in the blood, Sir W. Roberts recognises with Sir A. Garrod a partial loss of secreting power of the renal cell for uric acid only, and not for other constituents of the urine. Lead impregnation, or premature senescence, or any other 'depressors of the uric acid excre-

tion,' might readily lead to minute but cumulative daily arrears in the amount of uric acid removed, and saturation of the blood with urates would be inevitably induced.

In some individuals whose arrearage is habitual and inveterate, the frequency of the recurring attacks of precipitation into the fibrous structures is 'providential and protective.' In a second group the loss of adjustment is an infrequent and almost accidental 'mischance'; these are favourable cases in which persevering treatment will succeed in preventing a recurrence of precipitation, or in reducing its frequency and extent; but in the first group, the permanent character of the renal defect makes it 'vain to expect that we can redress the balance, and restore the equilibrium between production and elimination.'

'Gentle sprinklings' of the sodium biurate in its finest and most minute crystalline form, occurring in the most varied situations, would best explain the manifold visceral and neurotic disturbances noticed, as well as the 'pricking pains in the joints' induced in certain subjects by particular wines.

The Re-solution of Uratic Deposits.—This eventuality also finds its explanation in Sir W. Roberts' observations and theory. Assuming that, during the often long intervals between the outbreaks, the blood and the synovia regain their purity, 'since the solvent relation of the bodily fluids to the material of gouty deposits is simply a question of saturation or of subsaturation,' the sodium biurate will undergo re-solution; and it may chance that a joint formerly the seat of gout may, at death, present no trace of the biurate; indeed, this change may be watched proceeding during life in the pinna of the ear, where tophi are seen to come and go.

Conversely, a joint found infiltrated with biurates after death is not thereby proved to have been the seat of inflammation. It would be, of course, easier for fibrous tissues to be cleared of their deposit than for cartilages.

Precipitation of Uric Acid in the Individual Tissues.—We may now briefly review the subject of uratic precipitation with reference to the several tissues or organs.

In the *blood* itself, so long as it preserves its alkalinity, uratic precipitation is excluded. In an opposite phase of reaction, precipitation would occur so soon as an excess of uric acid chanced to accumulate. Of the occurrence of this combination of circumstances we possess at present no actual proof. Any precipitation which might conceivably occur in the bulk of the blood would be in the shape of very minute particles, and these would probably be dealt with, as most other floating material, by the scavenger cells, and disposed in any of the collecting organs.

The special liability of all connective tissues, but particularly of the fibrous structures within and about joints and of the articular cartilages, has been connected with the relative inactivity of their blood circulation, and with their dependence upon nutritional exchanges with lymph or synovia, both fluids being more susceptible of suffering locally a loss of alkalescence, and of solvent power for uric acid, than blood. Moreover, Sir W. Roberts has shown that synovia favours precipitation of biurate in a special degree, owing to its high percentage of sodic salts. The combination of an unvielding texture, as in cartilage and in fibrous tissue, with superadded pressure, as in movements of the joints, is probably an additional element both in the damaging effect and in the production of pain; much, however, of the latter is probably due to the tension induced by the contingent vascular and lymphatic engorgements. At any rate, a considerable amount of acicular deposit may exist in the cartilage without giving rise to pain.

The damage capable of arising from uratic deposit, as well as the pain, may be expected to be greatest where the circulation is least active, and therefore deposition is rendered easier and reabsorption more difficult.

The subcutaneous connective tissue is, next to the joints and their fibrous surroundings, the most common site for precipitation; and, as elsewhere described, the deeper layer of the cutis itself may be involved.

In the nerve structures and in muscle the deposit, when it occurs, is probably limited to the connective tissues, and any baneful effect felt by the special tissues would probably be communicated rather than direct.

In the *kidney*, the deposit is supposed to occur first in the connective tissue and lymphatics, and later in the tubes; and, except by Ebstein and others, the mechanical irritation set up by the biurate has been mainly credited with the destructive changes. Here, especially, the question of alternations between precipitation and solution assumes importance, if it be that the passage from one state to the other is, as suggested by Pfeiffer, fraught with risk to the neighbouring cells.

#### URIC ACID GRAVEL.

Our review of the subject of uratic precipitation would not be complete without a brief sketch of the subject of gravel, so closely allied, both chemically and clinically, to the subject of gout, and yet entirely distinct from it.

The factors in this condition are, (1) the rate of formation of uric acid, and (2) the rate of supply of its natural solvents.

In gravel, as in gout, heredity has a strong influence, which often determines the onset of the trouble in early childhood. In a paper on 'Renal Colic in Infants,' read

on January 14, 1896, before the Royal Medical and Chirurgical Society, Dr. R. A. Gibbons gives details of 'cases occurring in infants between nine and twenty-three months, in which all the symptoms of renal colic were present. In none of the patients was a distinct calculus found, but there was abundance of free uric acid, and small masses of mortar-like material passed consisting of uric acid; and the urine contained blood. In all the cases detailed there was a strong family history of gout. From the facts brought forward, it is clear that the affection is more rarely met with in the infants of the poor, and that the cause of this is due to the greater tendency to the inheritance of gouty conditions amongst the wealthier classes, the latter being more prone to the formation of uric acid, and to suffer from conditions classed under the name "gouty."

In children gravel is apt to produce intense restlessness, pain often in the umbilical or iliac regions, and considerable irritability of temper. There is often frequent desire to micturate, and ineffectual rectal tenesmus. Dr. Vaughan Harley, in a valuable paper on 'The Chemical Pathology, Symptoms, and Treatment of Uric Acid Gravel,'\* suggests that in doubtful cases the fresh morning urine should be centrifuged for crystals and casts, precipitation of uric acid being most likely to take place from the 'urina sanguinis' secreted after the alkaline effect of the last meal has long passed away. Any crystalline sedimentation within the tubules would lead to irritation of their lining cells, and probably to a formation of casts, and to the escape of albumin. Indeed, latent uric acid precipitation of this kind has been given as a frequent cause of functional or cyclic albuminuria.

<sup>\*</sup> British Medical Journal. March 23, 1895.

In the adult the symptoms described by Dr. Vaughan Harley are pain, like lumbago, extending down the ureters to the ovary or the testicle, with frequent desire to micturate.

Impaction of gravel in the ureters is often so painful as to simulate peritonitis, with vomiting, and even delirium.

Slighter symptoms are: 'tender feeling' over the loins, also a dull pain aggravated by any new position, and relieved only by lying in bed.

Radiation of the pain occasionally takes place, down the arms (Levison), usually down the legs, and especially down the front of the thighs, resembling anterior sciatica in causing the knees to be everted and the heels to be drawn up.

Irregularity of the heart is occasionally present, constipation usually so. Various neuralgiæ (migraine, angina, asthma, etc.) are also described by Da Costa.

## 2. THE MECHANISM OF PRECIPITATION OF URIC ACID IN URINE.

The views of Sir W. Roberts have already been described.\* The automatic splitting up of the quadriurate, under the influence of water, into uric acid and biurate (the latter being immediately converted into a fresh molecule of quadriurate by giving up half its base to the monobasic phosphate) would rapidly lead to a precipitation of the greater part of the uric acid, whereas normally no precipitation occurs. He connects its persistent solubility in normal urine with the presence of the urinary salines; and he specially insists on the influence of common salt in warding off precipitation, and attributes to its insufficient supply the frequency of uric acid concre-

tions among Hindoos, whose staple of diet is rice. He also points out the action exerted by the urinary pigments in the same direction.

A somewhat different explanation is set forth by Liebermann, who traces in the kidney substance an acid reacting body, acid-lecithin-albumin, capable of converting Na<sub>2</sub>HPO<sub>4</sub>, or other alkaline reacting salts, into acid salts, and in this way of changing the reaction of blood serum into the acid phase. By using a layer of this substance as a filter, these changes can be brought about in the chemical laboratory; and when an alkaline sodium phosphate solution is injected through the freshly-removed kidney of a dog, the outflowing fluid is found to be acid.

Meanwhile, the tissue CO<sub>2</sub> perpetually comes to rescue the acid-lecithin-albumin from its alkaline combination. Liebermann\* traces an analogy between the behaviour of the mucous membrane of the kidney and that of the stomach.

The acid of the urine would thus be conditioned by the available amount of acid-lecithin-albumin; and the available amount of alkaline phosphate would determine whether the soluble urates would escape being broken up by the renal epithelium; or whether the latter would split them up and cause a crystalline deposit in the tubules; or whether, lastly, the relative deficiency of phosphates, or the relative increase of urates, would lead to the latter being insoluble.

Liebermann further inquires whether the fact that the urine of herbivora is turbid and alkaline may not be due to the lecithin-albumin in their kidneys being insufficient for the task of turning into the acid phase the alkaline salts which they so largely take in.

<sup>\*</sup> Archiv. für die Ges. Physiologie, l., p. 55. Cf. Revue des Sciences Médicales, 1892, vol. xl., p. 444.

Tests for an Excess of Uric Acid in Urine.—The following rough test for an excess of uric acid in limpid urine is given by Dr. Vaughan Harley\*: A 'high-level' precipitate is normally produced by cold nitric acid in healthy urine, but only after standing from five to ten minutes. When the upper cloud forms in less than five minutes, the urine may be regarded as unusually prone to deposit uric acid; if, on the contrary, more than ten minutes should elapse, either the amount of uric acid is less, or its solvents are present in larger quantity than usual.

Pfeiffer's uric acid filter was supposed to be a test for the gouty character of urines, and to supply a proof of the existence of a relatively insoluble variety of uric acid in gout. A filter upon which o'5 gramme of uric acid is placed will, according to Pfeiffer, retain the uric acid of the gouty urine which is made to pass through the filter, that of a healthy urine not being retained, or only partly so. Healthy urine would require a much larger amount of uric acid on the filter (from 2 to 3 grammes). Feliziani's determinations do not support these statements. Half the number of gouty urines tried by him did not respond to the test, whilst many healthy urines responded to it. Sir W. Roberts has also shown that any urine, whether gouty or not, may be freed from uric acid by repeated filtration through the same uric acid filter.

### OXALIC ACID AND GOUT.

Sir A. Garrod,† who demonstrated the presence of oxalic acid in the blood in the course of gouty arthritis, and in two cases also in the sweat, regarded it as derived from

<sup>\*</sup> Loc. cit., p. 639.

<sup>† &#</sup>x27;Med. Chir. Trans.,' vol. xxxii., 1849.

the oxidation of uric acid—a view which is still held; though, as pointed out by Sir Dyce Duckworth, other sources must exist, as shown by the amount being often much larger than would correspond to uric acid. Its frequent association with uric acid in gouty urine is probably, however, nothing more than an expression of the close relationship between these two forms of acidity, and of the practical identity between the dietetic influences which led to them. Rhubarb, sorrel, tomatoes, celery, watercress, are all supposed to lead to oxaluria. According to Sir Dyce Duckworth,\* in addition to these, direct production may also be due to 'imperfect oxidation of saccharine, starchy, and oleaginous principles of food; to increased tissue metabolism, whereby the fatty acids found in excess are completely reduced; to excess of lactic and butyric acid, formed in intestinal dyspepsia, insufficiently reduced; to excess of mucin in the urinary channels, which tends to foment and favour deposition of oxalates; and to ingest of water rich in lime salts.'

Oxalate calculi, which are less frequent than uric acid calculi, are often partly made up of alternating layers of the latter. Prout thought they were apt to arise after an attack of gout. He pointed out that oxaluria was also apt to alternate with an increase in the phosphate, and especially in the phosphate of lime, which might amount to phosphaluria.

Boils and carbuncles are stated by Sir Dyce Duckworth to occur in oxaluria, as they often do in glycosuria.

Excess of oxalic acid is not directly responsible for any of the complications of gout; but the dietetic factors leading to it, the hepatic and gastric delicacy which may be its immediate cause, and the depression so often attend-

<sup>\*</sup> Loc. cit., p. 197.

ing upon it, are so many points of contact between two diseases which run parallel courses and occasionally overlap.\*

\* The latest contribution to this subject is an exhaustive paper on 'The Excretion of Oxalic Acid in Urine,' in the Journal of Pathology, vol. iii., January, 1896, by Dr. J. Craufurd Dunlop, who states that oxalic acid is a constant constituent of urine under a mixed diet, averaging '017 grm. per diem, and that its precipitation as calcium oxalate occurs in about one urine out of every three; that it is not a metabolic product, but is absorbed from the alimentary canal; and that oxaluria is essentially nothing more than the result of hyperacid dyspepsia.

### CHAPTER XIII.

### THE PATHOLOGY OF URIC ACID.

### IS URIC ACID TOXIC?

Many of the substances contained in the excretions are toxic, and act as poisons unless removed from the system without delay. Uric acid, minute quantities of which are normally present in the blood in soluble combinations, accumulates in perceptible proportion under the influence of gout. In gravel and calculus it occurs as a precipitate in the urinary passages, and in gout its crystalline salts are deposited in the parts affected. We naturally inquire whether in any of these forms it is capable of exerting a toxic action.

As a solid, wric acid itself is probably inert, and, being sparingly soluble, may lie for years in the kidney, ureter, or bladder. These are the only situations in which it occurs. In all other localities and circumstances (including the administration of pure uric acid), it is ultimately with the urates—and largely with the urate of sodium—that we have to deal. In the following remarks the term 'uric acid' should be understood to apply to uric acid and to its combinations.

The *urates* occur in the crystalline form in the gouty deposits (as sodium biurate)—as well as in solution in the blood and in the tissues (as quadriurates).

By most authorities the action of the solid biurate is

regarded as a purely mechanical one, and much of the destructive change observed in the joints and in the kidney is usually explained in connection with the irritating shape of the crystals. Mechanical conditions are, for Sir W. Roberts, a sufficient cause for the incidents of regular gout, and for their varying intensity, which would be determined by the amount and suddenness of the precipitation and by its situation in soft and loose, or in unyielding parts, such as the lobe of the ear or the joints respectively.

The insolubility of the biurate, although great, does not compare with that of uric acid; and it has been asked whether in the highest state of concentration, namely, immediately before or immediately after precipitation, a solution of the salt may not locally exert a toxic action. That fluctuations in the quality of the juices may at times lead to the deposits being slowly dissolved again is clinically proved in the case of tophi in the auricle, which may be seen to vanish, and anatomically by the roughened and pitted condition of the surface of cartilages, from which uratic deposit has been reabsorbed, occasionally found in joints which had formerly been the seat of unequivocal gout. The juices bathing the deposit which is undergoing solution may be fully charged with biurate. The question is thus narrowed down to the case of the urates in a state of solution.

Are Urates in Solution Toxic?—The view that urates are toxic in their soluble form has been strongly urged by two observers—Haig and Ebstein, and by the latter they have been regarded as toxic mainly in their semi-fluid or gelatinous state—that which immediately precedes their precipitation or follows upon their being redissolved.

According to Pfeiffer, a solution of pure uric acid injected under the skin acts as a strong irritant; but, as previously stated, uric acid never occurs in the living organism in this form. On the other hand, subcutaneous injections of urates, though they may set up some pain and irritation, entirely failed in his hands to produce necrosis.

Haig, who dwells with special emphasis on the nerve intoxications, has bestowed chief attention on the more soluble condition which uric acid assumes in its saline combinations in the blood. The disturbing properties of uric acid, even when it is guarded by combination with an alkali, is illustrated by a variety of sensations and symptoms, such as headache, neuralgia, general discomfort, depression, high tension of the pulse, etc., which, according to him, immediately disappear when the uric acid, being deprived of its alkali and precipitated into the collecting organs, becomes once more inert and non-poisonous.

On the other side, the latest supporter of the absolute innocuousness of uric acid, whether in solution or as a deposit, is Professor Bouchard, who adduces experimental evidence to show that the injection into rabbits of even large quantities of uric acid produces no other effects than those which belong to the injection of so much water, whilst the uric acid is not excreted as such, but in the shape of an increased output of urea. Similar experiments and conclusions had previously been arrived at by other observers.

Although large quantities of uric acid have been mixed with the food or injected into the veins of animals, the toxic actions ascribed by some to uric acid, in explanation of the phenomena of irregular gout, have never received experimental demonstration; neither does the gouty man, saturated with uric acid, present, on the eve of his attack, any of those symptoms which have been described as resulting from uric acid intoxication.

As suggesting a non-poisonous character for uric acid, Sir W. Roberts calls attention to the essentially nonpoisonous character of its homologue, urea. Drachm doses can be swallowed without any harm. According to Dr. Rose Bradford, 30 to 45 grains are always present in the human body, and often much larger quantities, without any toxic result.

In conclusion, there is distinct evidence that even large doses of uric acid fail to produce severe toxic results, though they may lead, according to Dr. Haig, to nerve discomfort and visceral symptoms. Evidence is still wanting to confirm Ebstein's statement that concentrated solutions of urates will lead to a necrosis of tissues.

## THE ACCUMULATION OF URIC ACID.

The accumulation of uric acid in the blood, Sir A. Garrod's fundamental fact, is universally recognised as part of the gouty attack, but it has never been fully explained. Sir A. Garrod's own explanation is that there occurs a temporary or a permanent renal inadequacy, a check to the excretion of uric acid, and that the latter accumulates in the blood and leads to all the symptoms of gout.

This is also the view adopted by Dr. Haig, though he does not limit the evil results of the circulation of uric acid to gouty symptoms, but traces to it many other troubles. In gout he estimates the yearly accumulation of uric acid in the body at 400 grains. Other observers, including Salomon\* and Von Jaksch,† have fully confirmed Sir A. Garrod's discovery.

The state in which uric acid is contained in the blood has not been experimentally determined; it is probably

<sup>\*</sup> Charité Annalen, 1878, p. 137. Salomon detected uric acid in the blood of three patients during the attack, but was unable to find any during the intervals.

<sup>†</sup> Ueber die Klin. Bedeutung der Harnsaure, 1890.

variable. It has hitherto been invariably admitted as a chemical necessity bound up with the alkalinity of the blood, that any uric acid it may contain must be present as a salt; and there can be no doubt that this is the usual condition. Still, in view of the elementary state of our knowledge of the blood, and of the acquired fact that the blood may be sometimes faintly acid, we should avoid any exclusive statement. Assuming that the uric acid generally occurs in the combined state, we are quite unable to define its precise chemical position and its relations to the plasma and to the blood-cells respectively. The chemical estimations tell us of its presence and state of concentration, nothing more.

In cases of inveterate chalky gout the behaviour of uric acid is well known. Whilst it is excreted in a diminished quantity in the urine, it collects in the gouty deposits; and, since its percentage in the blood is never considerable, we may assume that the local accumulation is derived rather from its retention in the system than from any excessive production. This conclusion does not, however, claim to be mathematically established; much less can we safely extend it to other forms and phases of gout. The question is still whether there may not be a hyper-production of uric acid in gout, and many attempts have recently been made to determine, by indirect methods, whether any special form of diet is capable of supplying it in excess. The practical aspect of these investigations in connection with the treatment of gout is obvious, and will justify a brief reference to them in subsequent pages.

Much older than experimental pathology is the wellestablished clinical observation that biurate will accumulate and form deposits in the poorly fed, even in those whose dietary includes little nitrogen. In them Sir A. Garrod believes that the accumulation is mainly due, and sometimes entirely due, to a retention, rather than to any increase in the production of uric acid.

Although the mode of origin and of accumulation of uric acid, and its vicissitudes in the blood and in the juices, are beyond our ken, there are two terminal situations—the urine and the gouty deposits—in which it can be not only got at, but readily estimated. It may also be caught during its passage through the blood, or extracted from the tissues; but here the determinations are less certain; neither do we learn much from them as to its site of origin.

As to the quantity present in the blood, Levison\* remarks that the daily amount of uric acid retained must be very small, or that the acid must be converted in the blood into soluble compounds, otherwise tophi would acquire a much greater size than that which is observed.

The amount of the excretion in gout may certainly be taken, on a broad average, as not exceeding the excretion of a healthy person; and it is apt to be either permanently or at intervals decidedly less. Camerer† arrives at the result that the excretion by gouty patients does not materially differ from the normal, and that in any case it is not increased above a healthy standard.

Pfeiffer,‡ in his determinations of the uric acid excreted, has reduced the amount found in each case to a uniform scale of 100 kilos of body weight. He believes that the physiological amount bears a definite relation to the age of the individual. In health he finds that the quantity diminishes progressively with age from a maximum of

<sup>\*</sup> Loc. cit., p. 45.

<sup>†</sup> Deutsch. Med. Wochenschrift, 1891, Nos. 10, 11 (quoted by Levison, loc. cit., p. 42).

<sup>‡</sup> Berliner Klin. Wochenschrift, 1892, p. 415 et seq.; cf. Levison, loc. cit., p. 42.

1'250 or 1'211 grammes per day during the first decade, down to 0'616 gramme at the age of sixty-five, and even to less at more advanced ages. In gout which has not yet become chronic, he finds that rather less uric acid is excreted than corresponds to the given age. In advanced tophaceous gout, associated with arterial disease, albuminuria, etc., Pfeiffer reports that there is, on the contrary, a slight increase.

### CHAPTER XIV.

## THE DERIVATION OF URIC ACID.

THE 'OXIDATION' THEORY OF URIC ACID.

SINCE the observations of Frerichs, and Wöhler,\* to the effect that uric acid was artificially convertible into oxalic acid, and ultimately into urea and carbonic acid, but that when introduced into the system as food or through the veins, it was not excreted as such, but was passed out in the urine as urea—an interpretation of the facts which has at a more recent date been again called in question—this body was long regarded as representing a stage in the oxidation of nitrogenous tissues and foods, and its occasional excess as the result of a delay at this stage of the oxidation. It was eventually shown that limitation of the oxygen supply, as in artificial interference with respiration (Senator), or as in pathological or experimental anæmia, did not increase the output of uric acid.

Not less significant is the inability of the oxidation theory to explain why the entire supply of nitrogen is not excreted as urea, and why the amount of uric acid excreted should be practically constant instead of being subject to accidental variations.

For this physiological regularity, and for the excessive excretion of uric acid which occurs as an individual

<sup>\*</sup> Cf. Dr. Vaughan Harley, loc. cit.

peculiarity in the subjects of gravel, Sir W. Roberts offers an ingenious explanation. The presence in some of the lower animals of urine consisting almost exclusively of uric acid, whilst the urine of the more highly evolved is almost free from it, suggests the thought that evolution may have gradually reduced in the latter the uric acid department of the excretory function to the proportions of a vestigial rudiment. Under the influence of atavism the lost function might in some individuals regain some of its ancestral importance.

Lastly, it would be difficult to explain on the oxidation theory the fact that the active respiration of birds and their aërial life leaves their nitrogenous excreta in a relatively unoxidized state.

# THE CLINICAL AND EXPERIMENTAL STUDY OF THE DERIVATION OF URIC ACID.

In the inquiry as to the derivation of uric acid, experiments can only afford an indirect help: what we need to know is the mode of production of uric acid in gout. An excess of uric acid induced in animals or in man by artificial means may or may not be due to the same mechanism as that peculiar to gout. Much as experimentation has taught us as to the chemical behaviour of uric acid in the body, so that we know more to-day about this than concerning gout itself, it has not elucidated the derivation of uric acid. We cling, therefore, with renewed appreciation to the few broad clinical and physiological facts which we can trust:\*

<sup>\*</sup> It should not be forgotten that, putting aside the few accurate determinations of the amount of uric acid in the blood, our estimate of the amount of uric acid produced in the system is based upon the amount which is found in the urine, and cannot be regarded as absolutely trustworthy.

- I. In health the daily quantity of uric acid excreted is small (from 8 to 12 grains), and it bears to the quantity of urea an almost constant proportion, estimated by Dr. Haig at I to 33, by others at I to 40, or even I to 45. The total amounts may vary; but they rise and fall in a fairly even ratio.
- 2. In some diseases the normal output of uric acid is much exceeded. Leucocythæmia sometimes increases it very largely. It is also increased in some of the diseases of organs influencing the constitution of the blood, and particularly of the liver and of the lungs, as in hepatic congestion and pneumonia, and in gravel.
- 3. An *increase* is sometimes seen also in the anæmia of underfed, overworked, or exhausted subjects.
- 4. A decrease of the excretion is observed in various other affections, including chronic gout, diabetes, chlorosis (in some cases), chronic kidney disease, some forms of hepatic disease, etc.
- 5. The physiological oscillations connected with variations in the quantity or in the kind of food, or of muscular or nervous exertion, usually bear no comparison in their degree with those due to disease.

Muscular exercise has a decided effect in increasing the output of uric acid, and this may be due to the leucocytosis attendant upon excessive muscular exertion. The excess may, however, be traced partly to increased acidity due to muscular work; and the possible influence of the nervous exhaustion which accompanies muscular fatigue should not be lost sight of.

Large quantities of water as a beverage do not occasion any increase (Schöndorff); but alcohol increases the output, perhaps owing to the leucocytosis which it induces.

Diet has a direct influence, the total excretion being at a minimum under vegetable alimentation, greatest under an animal dietary, and at an intermediate level with a mixed diet.

Animal proteids, according to Maruss (quoted by Dr. Vaughan Harley), cause a larger excretion than vegetable proteids.

Dapper's\* recent investigations prove once more that, as previously shown by Schultze,† a highly proteid diet, whilst it increases the absolute amount of uric acid excreted, diminishes its relative amount as compared with the total nitrogenous output.

In his own case, Dapper made successive observations on the amounts excreted; first, during a period of abundant proteid supplies with very little fat and carbo-hydrates; and, subsequently, during a phase of alimentation poor in proteids and rich in carbo-hydrates and fats. During the latter, both the total nitrogen and the uric acid fell, but the uric acid much less than the former. The amounts are shown below:

Urea per diem. grms.	Uric Acid per diem. grms.	Total Nitrogen.	Nitrogen as Uric Acid.
Nitrogenous diet 21'6	1,01	65	I
Chiefly non-nitrogenous diet 12.6	0.45	46	I

Similar determinations were made in the person of a servant, with the following results:

		Urea per diem. grms.	Uric Acid per diem. grms.	Total Nitrogen.	Nitrogen as Uric Acid.
Meat diet	 	 13.46	1.0	43	1
No meat	 	 9.817	0.012	32	I
Mixed diet	 	 14.75	0.788	56	I

<sup>\* &#</sup>x27;Dapper, 'Ueber Harnsäure Ausscheidung beim Gesunden Menschen unter Verschiedenen Ernährungs Verhältnissen" (Von Noorden Beiträge). Cf. Revue de Médecine, 1894, vol. xiv.

<sup>†</sup> Arch. de Méd. Expér. et d'Anat. Path., 1889, p. 871.

Here, again, therefore, the same rule applies: there is a relative increase in uric acid with the vegetable diet, although the total nitrogen sinks. The figures would seem to show that with a mixed diet the amount of uric acid is least, both absolutely and relatively, although the urea may be abundant.

These facts are in contradiction with Pfeiffer's idea that there exists a settled proportion between the body-weight and the amount of uric acid excreted. Dapper found that for 100 kilos. of body-weight the amounts of uric acid varied between 0.57 and 1.44.

Piperazine was tried in the second sets of experiments, 4 grammes being administered daily for three days. This took but slight effect on the excretions, the proportion being altered from 1—43 to 1—45.

## THE DERIVATION OF URIC ACID FROM NUCLEIN.

The work of Horbaczewski, of Kossel and of others, has opened up a fresh field for the study of the origins of uric acid. Horbaczewski\* found that uric acid might be derived from the decomposition of tissues, and with particular facility from that of the spleen. This discovery was a confirmation of a view conceived long ago by Parkes, and entertained since then by others.

The method adopted was the following: fresh splenic pulp was digested for 8 hours at 50° C. with 8 to 10 parts of water. When in the early stage of putrefaction the mass gives a filtrate which, after treatment with subacetate of lead and after sterilization, contains neither uric acid nor xanthine bases; but, if now boiled, it immediately gives

<sup>\*</sup> J. Horbaczewski, 'Beiträge zur Kenntniss der Bildung der Harnsäure und der Xanthin basen' (Monatshefte für Chemie, xii., pp. 221-276).

xanthine and hypoxanthine, but remains free from adenine or guanine.

If, instead of being boiled, the splenic pulp is allowed to stand (at 40° C.) in contact with some arterialized blood or with oxygen-water, or if it be merely exposed to an atmosphere of oxygen, it will ultimately be found to contain uric acid in the proportion of 0.0025 grammes for each gramme of pulp.

On the other hand, by artificial digestion of the spleen, pure nuclein may be obtained, from which, by allowing it to stand at 40° C. in contact with blood, uric acid will split off.

These observations were not limited to splenic pulp, but Horbaczewski found that a similar supply could be derived from the mucous membrane of the small intestine, from red marrow, from the thymus, from muscle, from the salivary gland, the gastric and intestinal mucous membrane, the pancreas, the liver, the lung, the brain, the kidney, the skin, the tendons, the cervical ligaments, the cartilages of the ear, etc., and from pus. They all yield xanthine, as an indication that uric acid could be likewise derived.

From these observations Horbaczewski argues that as the organs do not change sufficiently rapidly to account for the output of uric acid, the leucocytes, which are abundantly contained in the spleen, and also present everywhere in the tissues, must be the source of the nuclein. If so, uric acid would vary in its production according to the variations observed or induced in the aggregate number of leucocytes.

Experimentally, it was found that quinine and atropine, which both diminished the number of leucocytes, also depressed the excretion of uric acid, and that pilocarpine had the opposite effect on both; antifebrine and phenacetine, however, increase the one while decreasing the other.

Returning now to nuclein, Horbaczewski found that its injection into the veins largely increased the uric acid output. This fact, however, could not lead to any final conclusion, inasmuch as the same substance, when injected, increased the leucocytes as well; and the question remains undecided whether the increased production of uric acid is the result of the injection and arterialization of so much nuclein, or of the proliferation of living leucocytes to which the injection may have given rise.

Stadthagen appears to have obtained in dogs the opposite result—decrease of uric acid, increase of urea. Conflicting results have also been reported by various observers in connection with the direct ingestion of uric acid.

Our ideas as to the fate of any additional quantities of uric acid introduced into the economy thus remain in suspense. In leucocythæmia the vast increase in the number of leucocytes should, according to the nuclein theory, go hand in hand with an increase in the uric acid. The results obtained long ago by Bartels, as well as those of more recent observers (Schultze and Ebstein), fully confirm that surmise.

Fleischer and Penzoldt (quoted by Dr. Vaughan Harley) attempted a further proof by feeding a leucocythæmic and a healthy person on the same diet. The same weight of urea was produced in both cases from the proteid supply; but, over and above this nitrogenous output, the morbid urine contained double as much uric acid as the healthy.

According to these views, the conditions leading to an increase of uric acid would be practically those leading to a leucocytosis.

It had long been known that in health a varying degree of leucocytosis follows each important meal, especially if much proteid be taken. Maruss,\* starting from this obser-

<sup>\*</sup> Quoted by Dr. Vaughan Harley, loc. cit., p. 637.

vation, determined the amount of uric acid excreted at different periods, and found that, whereas urea excretion was slow to set in and slow to attain its maximum (as late as nine hours after the meal), the uric acid excretion (which was greater after animal than after vegetable diet) began early, and reached its maximum as soon as two to five hours after the meal, having by this time doubled or trebled its previous amount; after this, it gradually sank till the thirteenth hour of fasting, when it remained constant.

The results obtained by Chittenden and by Cameron, in animals and in man,\* also show a parallel increase in the leucocytes and in the amount of uric acid excreted.

The same result has been found to follow the ingestion of pilocarpine and of phosphorus, whilst quinine and arsenic have the opposite effect.

The greater proportion of white cells normally present in the blood of children, whose excretion of uric acid is decidedly greater in proportion to their body-weight than that of the adult, is an important physiological fact in the same direction.

In simple anamia the excretion is not increased, leucocytes not being present in excess. This adds weight to the inference derived from leucocythæmia, where the increase of uric acid is regarded as due to the vast increase in leucocytes. Other diseases, such as pneumonia, which cause proliferation of leucocytes, likewise lead to increased uric acid excretion.

Levison,† who agrees with Garrod and Roberts in regarding the accumulation of uric acid as due to deficient excretion rather than to hyperproduction, does not accept Horbaczewski's views as in any way applicable to gout. He states that gout is not attended with any leucocytosis,

<sup>\*</sup> Quoted by Dr. Vaughan Harley, loc. cit., p. 638.

<sup>†</sup> Zeitsch. für Klin. Med., 1894, xxvi.

and that therefore the nuclein of leucocytes does not enter into account. On the other hand, the uric acid excess in gout is not so great as in pneumonia and leucocythæmia. He seeks to explain this difficulty by the fact, demonstrated by Roberts, that the quadriurates require to be held in solution for some time to allow the biurate to be formed and deposited; healthy kidneys would eliminate the excess of urate too quickly for this.

## THE SEAT OF PRODUCTION OF URIC ACID.

The place of origin of uric acid has been variously held to be: (I) the kidney; (2) the liver; (3) the spleen; (4) the tissues in general, and in particular the connective tissues; (5) the leucocytes.

Zalesky's well-known experiments led him to conclude that the kidneys were the site of formation of uric acid. For, when the ureters were ligatured, no diminution was observed in the amount of uric acid, but merely a change in the locality of its storage. Being prevented from descending into its normal reservoirs, it ascended above the kidneys, which remained free except in their pyramids, where the tubes were blocked with it, and was deposited in the lymphatics and all the serous membranes except the meninges, in some of the small bronchi, in the heartmuscle, in the capsule of the liver, but not in the hepatic substance, and in the cartilages and the articular membranes and cavities. Specially noteworthy was its absence from the voluntary muscles and from the bloodvessels, although the blood, the bile, and other juices were freely charged with it, and its presence in the mucous membrane of the stomach and of the intestine.

On the other hand, when the kidneys of serpents were excised, although the period of survival was the same as

in the previous experiments (about twelve days), no uric acid was found to accumulate in the tissues.

Zalesky's conclusion from these experiments has been called in question, at any rate they cannot be applied in the absence of further proof to the case of mammalia and of man. In opposition to Zalesky, Schroeder has shown that in birds the production of uric acid is not limited to the kidney, but occurs in various tissues.

The view propounded by H. Ranke that the *spleen* takes a leading part in the formation of uric acid is supported by the fact that splenic enlargement in leucocythæmia is associated with an increased excretion of uric acid, and that quinine diminishes the excretion. It is important to note that the same increase is observed in lymphatic leucocythæmia.

Dr. Haig holds that uric acid is largely stored by the spleen under those circumstances which preclude its ready solubility and its ready circulation in the blood.

Professor Latham, as elsewhere stated, ascribes a share in the formation of uric acid to the kidney.

The liver has long been suspected of being the main seat of production, and many arguments have been adduced in support of this view. The experimental ligature or extirpation of the renal organs showed that many tissues share with the kidney the capability of forming uric acid, but that the liver possesses this power in a high degree. Meissner,\* in 1868, determined in birds that the amount of uric acid was always greater in the liver than in the blood.

Experimenting on geese, Minkowski† extirpated the liver, and during the six to twenty hours of their survival, found that 3 to 6 per cent. only of the nitrogen was then excreted

<sup>\*</sup> Quoted by Dr. Vaughan Harley, loc. cit., p. 638.

as uric acid, instead of 60 to 70 per cent. as in health. The nitrogen appeared to pass out in the shape of ammonia to the extent of 50 to 60 per cent., instead of 9 to 18 per cent. only during health.

Other important experiments, however, do not point to the liver as the chief producer.

Hahn, Massen, Nenchi, and Pawlow,\* ingeniously diverted the portal circulation of dogs into the *inferior vena cava*, thus shutting off the liver from the general circulation. The result of this experiment, which did not constitute so severe a measure, was that the uric acid output was greatly increased, although less urea was passed, the bulk of the nitrogen being eliminated as ammonium carbamate.

Nevertheless, the old view that the liver is a chief seat of production still holds its own, and clinical observation lends to it much probability, although the synthetical preparation of uric acid by Horbaczewski, and subsequently by Professor Latham, has not availed, as might have been hoped, to solve the question definitely.

We are led by these uncertainties to look more closely into the processes of assimilation. There is a yet earlier function than that of the digestive glands, performed by elements possessed of multifarious activities, and which are ubiquitous. The *leucocytes*, which are in respect of their locomotion, and perhaps in respect of their intracellular movements, among the most active constituents of the body, stand in a close relation to the process of alimentation. It is well known that they undergo a remarkable multiplication after meals and are obviously concerned with the work of elaboration of food as well as with that of purification of the blood. They are in great measure the

<sup>\*</sup> Quoted by Vaughan Harley, loc. cit., p. 638.

food carriers; and in the special form of overfeeding which ultimately leads to gout, they must be the first to experience the saturation with nitrogenous surplus which overtakes all the fixed elements of tissue. If the effect on the latter is a diminished vitality, a lessened resistance, and a degeneracy, we may expect to find the same tendency carried out in them to a much higher degree, and perhaps resulting in earlier decay and destruction.

To what extent they may have a share in the manipulation of the excess of uric acid circulating in the blood is beyond the range of speculation. In their capacity of scavengers they are hitherto known to deal only with solid particles. This, of course, need not exclude an absorptive or selective power for substances in a state of solution; but of this we know nothing.

On the other hand, they stand in a peculiar relation to uric acid, which has been pointed out by Horbaczewski. Nuclein, of which their nucleoli consist, can be made to yield uric acid, and in this we possess a source of uric acid the supply from which might conceivably vary with the rate of cell reproduction and decay. The life history of the leucocytes might in this way be intimately connected with oscillations in the amount of uric acid set free in the blood or withheld from it.

These speculations, though they are as yet imperfectly supported by observation, may serve to illustrate the idea of the bio-chemistry of uric acid as opposed to the purely chemical description hitherto given. They afford us insight into the vital or dynamic aspect of the problem, which the present theories, and in particular the theory of renal inadequacy in gout, have perhaps not sufficiently taken into account. Brown Séquard's discovery of the process of internal secretion and the discovery of chemotaxis and of phagocytosis suggest novel directions for our

theories and experiments. We now recognise in cells, and particularly in leucocytes, activities far beyond those of simple imbibition and assimilation. Uric acid may come within these spheres of influence. It is now conceivable that the non-excretion at the kidney may be due less to a renal block than to some more active retention, for which cellular attractions may be responsible.

# THE MORBID ANATOMY OF GOUT.

## CHAPTER XV.

## THE ARTICULAR LESIONS IN GOUT.

In spite of the variety of its clinical symptoms, general or constitutional gout cannot hitherto claim to possess a morbid anatomy of its own. The visceral lesions often associated with it occur yet more frequently in its absence, and are not specifically gouty. Sodium biurate and the consequences of its deposition are the only specific changes to be found under the scalpel, and they belong to local gout, the morbid anatomy of which should be dealt with as a strictly separate study. The whole subject is thus divided into two sections: (I) the affections of the joints, cartilages, bones, and fibrous tissues connected with a local deposition of the biurate, including also the deposits found rarely in other situations; and (2) the general changes connected with constitutional gout and gouty cachexia, and any visceral lesions incidental to gout.

(I) There is most to describe in the anatomy of chronic deforming gout, and this was long ago described by the ancients, even to the concretions or pultaceous accumulations found in the cavities of the joint. The changes in the earlier cases, or in inveterate gout without much

deformity, were not accurately known until modern times. We owe to Garrod the demonstration in them of the presence of sodium biurate in the cartilages and other joint structures. The uratic lesion is therefore regarded as present both in the acute and in the chronic stages, and the question arises, Is it ever absent where gouty symptoms occur?

In the joints biurate is deposited within the cartilage in the shape of extremely fine needles, and may also be found external to it in the synovia. Outside the joints it is deposited in the surrounding fibrous structures and tendons. Destructive changes may gradually occur in the same joints, and, if progressive, may lead to considerable deformity, and ankylosis; but outside the joints the accumulations of uric acid may be extensive without inducing necrosis. These outer deposits, disfiguring and to a certain extent crippling, although usually painless, are known as tophi. The skin over them may be so much atrophied and so greatly stretched as to ultimately ulcerate, when complications may arise.

(2) Visceral deposits of biurate have been found quite exceptionally. The only visceral changes occurring with great frequency are degenerative lesions in the kidney and in the bloodvessels; but renal cirrhosis and arterial atheroma are both commonly present in other conditions quite apart from gout, and are then, as in gout, apt to lead to cardiac disease.

## THE ARTICULAR STRUCTURES.

The small joints are first involved, beginning with the toe, then the metacarpo- and metatarso-phalangeal joints, the tarsus and the carpus, and, lastly, the large joints. In an unusual case mentioned by Garrod this rule was

departed from, and the hand was not involved, though the knee was affected. In general, the more attacks there have been, the more widely will the implication of the joints extend. This suggests the inquiry: Could gout itself be checked as a constitutional ailment by checking the local attacks? That this might be the case has been often suspected, and Garrod's theory almost directly leads to this conclusion.

### CARTILAGE.

Of all the joint structures, the cartilages are the first to exhibit the characteristic uratic deposit, either as a fine white superficial incrustation, or as a diffuse infiltration of the matrix and of the cells, and occasionally as a deposit in the deeper layers. Anatomical and chemical explanations have been offered for the special liability of cartilage. The chemical theories need not be mentioned again. The anatomical and physiological explanations are based upon the extravascular nutrition of the tissue, and its proneness to suffer from the effects of pressure or contusions.

The cartilage first shows stains, striæ or dull patches, and, lastly, the characteristic deposit in its thickness. At first the smoothness of the surface is not interfered with, though a fine deposit of biurate may be visible, showing that the earliest deposit need not be superficial. Later, unevenness or pitting may alternate with smoother patches; but the destruction is progressive, and ultimately the cartilage may disappear and the joint become filled with a plaster-like mass, and its structures disorganized.

Whilst atrophic changes and erosion are proceeding in the articular cartilages, hypertrophic outgrowths develop at their free margins. The 'lipping' observed in so high a degree in rheumatoid arthritis is a feature common to all forms of chronic arthritis, and is also found in gout. According to Dr. Wynne,\* the marginal outgrowths in gout are true exostoses, and not, as previously thought, ecchondroses, as in rheumatoid arthritis.

As to the exact localization of the biurate, Budd believed that the early white striæ were central, not peripheral; and it was considered that the vascular synovial fringes and the insertion of ligaments, being better supplied with vessels and possessing a higher vitality, were less obnoxious to the deposition.† According to Rendu, these situations are not exempt, and, indeed, sometimes they present peripheral fibrous bundles obviously connected with a process of peripheral irritative overgrowth. This author regards the deposit as probably a simple interstitial incrustation encouraged by weakness of circulation, as in senile calcification.

Sir Dyce Duckworth has arrived at the following conclusions: 'There is no special microscopical condition of cartilage peculiar to gouty deposit; the common site of deposit is at the free surfaces; but it may occur at any point, and the cells are not *foci* of deposition.'

Anatomical investigations have thus led him to the same results, in connection with the superficial deposits, as those derived by Sir W. Roberts from a chemical study of the question. He was not able to identify the necrotic changes described by Ebstein; though, after washing out the deposit, a granular appearance was found in the cartilage, actual destruction being present only where the deposits were very abundant. The superficial zone of the cartilage is the first to disappear. The more advanced lesions, such as proliferations of the cells, fibrillations of the matrix, and erosions which may expose the bone, are sometimes seen, independently of gout, as senile changes.

<sup>\*</sup> Cf. Duckworth, loc. cit., pp. 76, 77.

<sup>†</sup> Cf. Roberts, loc. cit. ‡ Loc. cit., p. 67.

On the other hand, uratic incrustation of the cartilage is sometimes observed where declared gout has not existed during life.\*

Ebstein contends that crystallization of the biurate in the cartilages is always secondary to some previous disintegration of their tissue. The same view had been stated, though less categorically, by various observers. Parkes had conceived the idea that uric acid was generated locally from the degenerating tissue. Laycock also favoured this view.

Ebstein's views are to a certain extent supported by such opinions as that of Bowlby, viz., that urates are never deposited except in damaged cartilage, and that some of the salt may arise from disintegration of the cartilage; and of Cantani, who supposes preliminary disturbance in nutrition of the joint, and thinks that, as set forth by Robin,† gelatinous structures may suffer transformation into uric acid.‡

#### BONE.

Within the bones changes are not usually present at first. The proliferative osteitis of the dense bony layers, and the associated rarefying osteitis of the spongy parts, to which the enlargement of the bone-ends is due, are, in the great majority of instances, secondary inflammations. Cruveilhier had described spontaneous deposition of urates in bones, and Rendu§ mentions a case related by Féréol. Garrod, however, does not accept its independent implication, but merely an extension within it of the deposition beginning in the joint. But, according to Duckworth,\*\*\*

<sup>\*</sup> Cf. Duckworth, loc. cit., p. 64.

<sup>† &#</sup>x27;Dictionnaire de Médecine,' 1865.

<sup>‡</sup> Cf. Duckworth, loc. cit., p. 64.

<sup>|| &#</sup>x27;Union Méd., 1869, p. 289.

<sup>\*\*</sup> Loc. cit., p. 70.

<sup>§</sup> Loc. cit., p. 22.

<sup>¶</sup> Loc. cit., p. 210.

BONE

uratic deposits have been repeatedly observed within the bone, independently of any affection of its cartilaginous covering.

In cases of long standing, degenerative changes occur in the bony substance, perhaps in connection with disuse, the spongy tissue becoming rarefied and greasy, and the marrow cells fatty. More definite and truly distinctive are the early and the late changes observed in the jointends of the long bones. Heberden's nodes are relatively early manifestations in a certain class of cases in which gout pursues a slow and almost latent course, and may never culminate in an acute attack. Their presence is a help to diagnosis; but, inasmuch as they may occur in other associations—indeed, Heberden himself denied that they had any connection with gout—they should never be regarded as conclusive, but considered in conjunction with other indications.

The late changes are the lipping of the rim, and the not infrequent synostosis of the articular surfaces of the bones. The bony nature of the marginal outgrowths, the bony ankylosis, and the absence of the eburnation special to osteo-arthritis, are characteristic skeletal features of gout, and enable us to identify the disease from the mere inspection of bones long buried.

The occurrence of total ankylosis is facilitated by the incrustation and stiffening of the ligaments, conditions which yet more often lead to a spurious ankylosis.

# THE FOINTS.

After the cartilages, the synovial membrane, the ligaments and tendons, and the connective tissue become affected, and the bone may also be the seat of deposition, though this is not the rule.

The process of deposition can remain latent only when limited to the articular cartilage. On the other hand, the cartilages may show after death, in cases with an undoubted gouty history, absence of biurate, but a pitted condition indicative of its former precipitation. This condition is distinct from the abrasions and erosions not uncommon in the cartilages of the aged, but thought to be more frequent in gouty than in other subjects. The general absence of tophi and of external deposits where the cartilages are extensively infiltrated has been pointed out by Dr. Norman Moore,\* as well as the occasional absence of intra-articular deposits in nodular joints, the ligaments of which and the adjacent tendons may contain biurate crystals. Some of the large joints, especially the knees and ankles, are prone to gouty arthritis; others, and particularly the hip and the shoulder, as long ago observed by Garrod, are remarkably exempt. We owe to Dr. Norman Moore† an elaborate analysis of the relative liability of the various joints in a series of eighty cases examined after death:

(1) Whenever urates are present in any one joint, degenerative changes usually are found in the same joint or in other joints of the same body. (2) Deposits of urate of sodium resemble other degenerative changes in being usually more or less symmetrical. (3) The deposit is more often found in the joints of the legs than of the arms. (4) Nearly all the joints of the lower limb may be affected, and none of the upper. (5) The metatarso-phalangeal joint of the great toe more often presents the deposit than the phalangeal. (6) However abundant in and below the knees, a deposit is rare in the hip-joint. (7) The great toes and knees often present a deposit when the ankles are

<sup>\*</sup> Cf. Duckworth, loc. cit., p. 69.

<sup>† &#</sup>x27;St. Bartholomew's Hospital Reports,' vol. xxiii., 1887.

free from it; but the ankles never present it if it be absent from the toes and knees. (8) When present in the ankle, the deposits usually also affect the ligaments of the foot. (9) A deposit in the wrist is accompanied with one in the elbow-joint. (10) The sterno-clavicular joint rarely shows deposit. (11) The articulation of the larynx rarely presents any deposit.

Articular cartilages may be heavily affected with deposit without any external deposition, such as tophi. Urates are sometimes not found in the interior of joints which have become nodular, though specks of deposit may be found in their ligaments and adjacent tendons. The immunity of the hip-joint and of the shoulder-joint are specially to be noticed.

The deformities of the hands in chronic gouty arthritis, apart from tophi and nodular enlargements, are not essentially different from those described by Charcot in rheumatic cases. They are made up of a lateral deflection of the fingers towards the ulna, and of a flexion of the proximal phalanx towards the palm, with or without a like flexion of the terminal phalanx, the middle phalanx remaining in extension. The bending of the fingers is satisfactorily explained in connection with the contraction of the palmar fascia, and with the uneven antagonism of the flexor and extensor muscles. Among the factors of deflection, attention may be drawn to the influence, in the act of prehension, of the pressure of the thumb, which is usually not affected, on the fingers, and especially to the considerable and constantly recurring pressure thrown upon the radial border of the index in rising from the recumbent or sitting posture.

In the *ligaments* the deposits take various forms, dotted, streaky, or diffused. Even in the *synovial fringe* deposits may occur, viz., in its subepithelial and subserous layers.

Rendu concludes that in all situations they tend to be localized, as in the case of the tophus, in the depth of parts.

The synovia may be clear, as in the earliest cases, or, more rarely, milky; or it may be coloured with blood. Its reaction is neutral or alkaline, but occasionally, as observed by Garrod (Observation 7), it may be acid. Where, as so often occurs, a biurate is precipitated in the synovial fluid, its origin may be attributed to two sources, the synovia or the incrustations.

Although relatively passive, cartilages and fibrous tissue ultimately react to the irritation, and a subinflammation arises. A double change takes place in the cartilage—a new formation, or ecchondrosis (Virchow), and a destructive ulceration of the surface by attrition. As a consequence of the latter change, severe destructive lesions arise in the larger joints, knees and ankles. In the smaller joints total incrustation may occur, and there may remain practically no cartilage, no synovia, merely a mass of plaster-like deposit extending from bone to bone and from ligament to ligament.

# THE PERI-ARTICULAR TISSUES, LIGAMENTS, FIBROUS TISSUES, TENDONS, AND BURSÆ.

Next to the cartilages themselves, the ligaments and the fibrous tissue protecting the joints, the synovial sheaths of the tendons, and the neighbouring bursæ, are specially prone to the deposits; and we might therefore expect a special liability to gouty lesions in joints (as in the hands and feet) possessing complicated ligaments and an abundant fibrous environment, with many tendons.

Peri-articular deposits in the fibrous tissue adjoining the articulations are often of considerable thickness. In well-

marked and inveterate articular gout the surrounding fibrous tissue may become impregnated with biurate, and the tendons likewise.

The peculiar attitude and deformity of the gouty hand are often due to the implication of the sheaths of the superficial and deep flexors. Dupuytren's contraction, in which the palmar fascia, and the sheaths, but not the tendons, are affected, and the analogous contraction of the plantar fascia, are very commonly met with in those who are free from the major manifestations of gout; and much discussion has arisen in connection with the ætiology of these lesions, and, in individual cases, as to the presence or absence of the disease. In the lower limb the tendo Achillis and the peronæi are specially liable.

At a distance from joints, in situations where it is exposed to much pressure or cold, and particularly in the palmar and plantar fasciæ, fibrous tissue is independently liable to gouty deposits or to gouty inflammation. Dupuytren's contraction is, with Heberden's nodules, among the symptoms of an ill-developed and very chronic variety of gout.

Bursæ are well known to be liable to gouty inflammation, quite independently of any concomitant arthritis, but the two affections may coincide. 'Crab's eyes' is the name given to small cysts, probably bursal, apt to form over Heberden's nodules or behind the nail.\* Bursæ, such as those of the metatarsal bones, and particularly of the great toe, of the heel, knee, and olecranon, are specially liable to incrustations and thickening from gouty inflammation. Those over the ischium and trochanter are, like the hip-joint itself, rarely affected.

Gouty bursitis claims importance in connection with peri-articular and intra-articular suppuration. Suppuration

<sup>\*</sup> Cf. Duckworth, loc. cit., p. 83.

of the gouty joints being unusual, whilst bursal abscess is fairly common, and is sometimes seen in gout where the neighbouring joints contain no pus, the formation of an abscess as a late event in gouty arthritis is regarded by some as always occurring from an extension of a bursal abscess.\*

# HÆMORRHAGE, SUPPURATION, AND GANGRENE.

Free hamorrhage into gouty joints has been seldom recorded; but a slight oozing of blood from a congested synovial membrane not infrequently stains their contents.

Suppuration is not the normal tendency of gouty inflammation. Nevertheless, in a few cases, pus may form in connection with some unusual irritation in the inflamed part. As previously stated, this is more often seen in a gouty bursa than in gouty joints. In the latter the fluid may present a puriform appearance, owing to the presence of loose urates in the altered synovial fluid, and the irritation produced by them may lead to the admixture of a little pus.

The non-suppurative course observed in the frequently spontaneous process of outward discharge of tophaceous matter is significant of the relatively slight proneness of gouty tissues to suppuration.

Gangrene does not occur in sthenic gout. It is mainly observed in advanced gouty degeneracy, and especially under the influence of senile atheroma or diabetes, its determining cause being generally some accidental lesion or pressure. It may, however, be the accompaniment of a direct arthritis: an instance of this kind is given by Duckworth,† without, however, any particulars.

<sup>\*</sup> Cf. Ollivier, quoted by Rendu, loc. cit., p. 26.

<sup>†</sup> Loc. cit., p. 83.

#### TOPHI.

Subcutaneous uratic infiltration of the connective tissue, involving the deeper layer of the derma, is apt to lead, in the worst cases, to a stiff hide-bound condition; the ulceration of these diffused infiltrating deposits is troublesome in proportion to their extent.

Localized subcutaneous tophi are to be looked for in two situations. Lecorché has described their occurrence as minute deposits in the thickness of the skin of the palmar aspect of the fingers, where they are apt to ulcerate and leave characteristic scars. Still more common and diagnostic are the tophi (present in one-half of the cases according to Garrod) in the helix or antihelix of the ear, or in the groove between them. Various other situations may present deposits—the eyelids, nostrils, or even the cheek, the skin of the fore-arm along its ulnar border, that of the shin, sometimes the skin of the thigh, or that covering the corpora cavernosa.\*

The chemical composition of tophi is somewhat variable, especially in respect of the amount of sodium and calcium urate; it is estimated by Sir Dyce Duckworth at about 10 per cent. of sodium chloride, and 50 per cent. of the biurates, with some calcium phosphate and animal matter.† According to Sir A. Garrod, they consist essentially of crystallized sodium urate, and the lime is only an accidental constituent. Sir Andrew Clark reported in one case a large amount of calcium oxalate, and believed in the frequent presence of calcium urate crystals. From all accounts, the deposits are therefore liable to variations, and calcium is seldom absent, although its quantity may be small. The consistency of a tophus is also variable; unlike the pure calcareous deposit, it tends to soften with

<sup>\*</sup> Cf. Rendu, loc. cit., p. 28.

age. In those cases where it ultimately disappears, we observe a gradual return towards the soluble state in which it was originally deposited.

According to Rendu,\* Tennant and Pearson were the first to demonstrate uric acid in gouty deposits. Fourcroy† and Wollaston‡ confirmed this discovery, and showed that they almost exclusively consisted of urate of soda. Later observations have shown that the composition may vary slightly, but is for the greater part sodium biurate, with which is generally mixed a small amount of calcium urate, some sodium and potassium chloride, and organic matter. Applied to gouty deposits the term 'chalky' is a misnomer; for, as shown by the absence of effervescence on adding acid to them, there is no carbonate of lime. Phosphate of lime, when found, is probably derived from the softened bone substance.

The reagents to be employed in examining the deposits are: hydrochloric acid, which shows the absence of effer-vescence, and therefore of calcium carbonate; nitric acid, with which the murexide test is performed; ignition, to identify the organic nature of the deposit and to separate the ash; nitrate of silver, which shows in the latter the presence of chlorides; and lastly acetic acid, which dissolves the biurate and precipitates from it the uric acid.

<sup>\*</sup> Loc. cit., p. 28.

<sup>† &#</sup>x27;Système des Connaiss. Physiques,' t. x., p. 267.

<sup>‡ &#</sup>x27;Philos. Trans.,' 1797, p. 386.

## CHAPTER XVI.

# THE CARDIAC AND VASCULAR LESIONS IN GOUT.

#### THE HEART.

WE should expect in association with gout pre-eminently those cardiac lesions which are related to organic or to functional vascular disease, and particularly to granular kidney and arterio-capillary fibrosis.

Pericarditis may occur in gout, but chiefly as a chronic change. In gouty-renal cachexia it is sometimes a fatal complication. It is noteworthy that Dickinson found recent pericardial changes in 16 out of 68 cases of granular kidney from all causes; and Dr. N. Moore in 80 cases of gout noted them in 12 instances, all being cases of granular kidney.

The myocardial changes are either those of fatty degeneration, or more commonly those of hypertrophy. Rendu\* asserts that granular kidney, when due to uratic gout, instead of leading to the customary hypertrophy of the left ventricle, is associated with a thinning of the wall and a tendency to fatty infiltration and to fatty degeneration. The cases to which he refers must have belonged to the class of coronary disease. In any given case the variety of the myocardial lesion may be said to depend upon the state of the kidneys and of the coronary vessels.

Gouty endocarditis can only be described as a slow fibroid degeneration affecting mainly the free edges of the valves, and gradually causing them to thicken and to shrink.\* The undoubted association between this change and gout is an important pathological fact, to be correlated with the yet more frequent association between rheumatism and sclerosis of the valves. It is, however, in gout a far more gradual and chronic process than in rheumatism, and commonly it is associated not only with the usual uratic joints, but with gouty degeneration of the vessels.

Uric acid has only rarely been found in connection with the heart. Garrod detected it in gouty pericardial effusion. Ebstein's case is the only recorded instance of a uratic deposit in the myocardium; degenerative cellular changes were also found in the vicinity of the nodules. An infiltration of the cardiac valves with biurate has been described from time to time. In the case reported by Sydney Coupland† the aortic valve was affected—the mitral in Lancereaux's two cases.‡

#### THE ARTERIES AND ATHEROMA.

Whilst true uratic deposit has rarely been reported, arterial disease, or, to call it by its pathological name, atheroma of the deep layer of the intima, is exceedingly common in gout. The preference shown by atheroma in

‡ Gaz. Méd. de Paris, 1868, p. 187, 'Traité d'Anat. Path.,' t. ii., p. 729.

<sup>\*</sup> Murchison, quoted by Duckworth, *loc. cit.*, p. 109, regarded arterial atheroma of early life and non-rheumatic aortic valve disease as occurring chiefly in the subjects of uric acid dyscrasia or of gout.

<sup>+</sup> Lancet, March, 1873.

<sup>§</sup> Landerer, Buchner's Report, bd. xiv., p. 60, 1847; Bramson, Zeitsch. für Rat. Med., 1845, t. iii.; Bence Jones, Lancet, 1856-Cf. Rendu, loc. cit., p. 36. Dr. Norman Moore has described uric acid deposits in the renal artery itself. Cf. Duckworth, p. 109.

this disease for the coronary and for the cerebral vessels is fraught with much clinical and pathological importance.

The great liability to cerebral hæmorrhage and to degenerative cardiac disease, both of which belong to an advanced stage of the vascular degeneracy, adds special interest to the rarity of aneurysm. Again, in spite of the tendency to arterial obstruction which would result from atheromatous thickening, arterial thrombosis and gangrene from thrombosis are rare (Duckworth), in striking contrast to the frequency of thrombosis in the veins.

The Ætiology of Atheroma.—The close association of chronic gout with chronic disease of the kidney explains the special liability of gouty subjects to arterial disease. Inasmuch as vascular atheroma is common among those whose interstitial nephritis has no connection with gout,\* nor with a gouty family history, we cannot regard chronic endarteritis as specifically gouty, but we recognise its direct ætiological relation with renal disease. At the same time, the constitutional influences which so largely determine kidney trouble among sufferers from gout may favour in them arterial degeneracy over and above the proportion normally traceable to kidney disease. This impression finds strong support in the tendency to arterial degeneration so often traced, like gout itself, through several generations. If both tendencies should happen to be simultaneously inherited, they could not but aggravate each other; and, independently of any such double inheritance, it is conceivable that a gouty cachexia might intensify the arterial changes special to kidney disease.

Peter has applied to atheroma the expression rouille de la vie; but the idea of the 'rust of life' is perhaps more applicable to gout itself, with its premature degenerative

<sup>\*</sup> It is significant that Professor Osler, who has noticed the great prevalence of atheroma in Baltimore, has very rarely met with gout.

changes and its freely circulating débris. Atheroma is found in all conditions of renal inadequacy, leading to autotoxis, as well as in habitual toxæmia ab ingestis (alcohol, lead, etc.), and therefore pre-eminently in gout also, where both are present. The ætiology of atheroma is too extensive to be fully discussed in these pages. The prevailing view is that it arises from excessive intra-arterial pressure, and as an inevitable senile change; but the writer has long felt that evidence does not absolutely warrant such a conclusion. It should be borne in mind that the causes which bring about the increased pressure have the earliest opportunity of exerting a direct influence on the intima itself which is in contact with the blood.

It has been suggested: (I) that the intima is, as it were, caught between the anvil and the hammer; (2) that the vasa vasorum are flattened by lateral pressure, and that the intima thus suffers malnutrition. These explanations are almost too mechanical. Do they apply in the case of syphilis? Dr. Oliver's studies with the arterial pressuregauge suggest that they may; for he finds in syphilis that absence of the reaction to posture, which he identifies with increased arterial tension. On the other hand, we have here an obvious toxic factor; and the same may be said of gout, of kidney disease, and of all conditions due to a contamination of the blood from excessive alimentation, or to an imperfect oxidation and emunction, as in visceral torpor. Dr. W. A. Hollis\* has recently put forward the view that atheroma may be originally due to bacterial and other impurities in the blood, the lining membrane becoming subsequently infiltrated with the retiring swarms of phagocytes. He also explains its special localization at the mouths of the smaller arterial branches in the aorta.

<sup>\* &#</sup>x27;Atheroma,' Journal of Pathology, vol. iii., No. 1, November, 1894, and No. 4, January, 1896.

The special liability in gout of the coronary and cerebral vessels is suggestive in an ætiological sense. Both these vascular systems are largely dependent for their oscillations in pressure upon the influence of general muscular activity. The latter may be regarded as periodically increasing the tension within the cerebral and coronary vessels in connection with the variations in the blood capacity of the contracting muscles; the relief afforded to the overworked nervous system by muscular work has, indeed, been attributed to this agency. The neglect of muscular exertion, absolute or relative, which is a recognised factor in the production of gout, might, if these views be correct, be held in part responsible for the degenerative changes occurring with undoubted frequency in the cerebral and coronary arteries of the gouty.

In its ætiology, gouty atheroma is probably not essentially different from other forms, and not the product of a specific gouty endarteritis. Here, as elsewhere in gout, we have to deal with faulty nutrition and its results; the impurity of the blood may act as an irritant to the arterial lining, and the latter is more prone to resent the irritation because participating in the malnutrition from which all the tissues are more or less suffering. The constriction of the vasa vasorum and the permanently raised arterial tension, though they may not be the most essential factors, must nevertheless be considered as contributing largely to the arterial degeneration, since the stress is thrown upon already weakened structures.

#### THE CAPILLARIES.

In all diseases of malnutrition the mischief concerns the infinitely small. With the naked eye we can only trace the coarse lesions. A study of the capillaries would bring us nearer to the seat of trouble. This study has yet to be undertaken, and for the present we can only infer that capillary malnutrition, impairment of function, and degeneracy precede the degeneration of tissues in general (with the notable exception of the extravascular tissues such as cartilage, the relatively early decay of which confirms the view that degeneration begins in the intimate structure of cells). The nutrition of the capillary wall undoubtedly suffers in sympathy with that of the tissues on the one hand, and with the arterial degeneration on the other. Evidence of deficient resistance is sometimes given in the occurrence of capillary hæmorrhages from the synovial, but especially from the mucous membranes. Hitherto, however, no specially 'gouty' change has been traced in the capillaries.

## THE VEINS AND PHLEBITIS.

The affections of the veins constitute an important chapter in the clinical history of gout; but there is comparatively little to note in their morbid anatomy. Atheroma is not a disease of veins. Uratic incrustations, which are regarded as rare in the arterial system, may, however, occur, though with yet greater rarity, in the veins.

Schroeder van der Kolk relates an instance of this kind in which the valves of the veins were also incrusted; the arteries were not the seat of this change.

The veins are conspicuously affected, not only during the gouty paroxysm, which by some has even been described as a 'phlebitis,' and which always occasions a dilatation of one or more of the superficial veins, but also in the shape of chronic dilatation and thickening, and of the acute thrombosis usually, and probably with good reason, regarded as due to a gouty phlebitis.

It might be possible, as suggested by Rendu,\* to draw

<sup>\*</sup> Loc. cit., p. 37.

a clinical parallel between the gouty atheroma of arteries and the atony and varicosity so often seen in the veins of the gouty, and to trace these likewise to a disease of the vasa vasorum; but the writer is unable to view the tendency to dilatation and to resulting cedema as 'direct consequences' of a gouty 'diathesis,' whatever may be meant by that term. As in the case of the arteries, the yielding of the vessel wall is in great part due to malnutrition, coupled with the increased venous fulness and pressure due to hepatic congestion, itself the outcome of faulty diet and deficient exercise.

The venous circulation is almost entirely carried on by lateral pressure. Any circumstance, and, above all, well-regulated exercise, raising the general tone and firmness of the surroundings of veins, helps the circulation within them, and saves them from distension. On the other hand, direct innervation enters largely into the question of venous tone; and this is equally manifest in the yielding of the subcutaneous veins from excessive fatigue, and in the opposite effect produced by rest, or, in an eminent degree, by change to a bracing atmosphere.

# VISCERAL HÆMORRHAGES IN GOUT—CEREBRAL, PULMONARY, AND OTHERS.

The hæmorrhages from varicose veins, from hæmorrhoids, from the bladder, and in the so-called hæmorrhagic retinitis, of which Mr. J. Hutchinson has investigated the relations with gout,\* need only a passing mention.

Cerebral Hæmorrhage.—As in non-gouty granular kidney disease, the brain is the most common seat of arterial rupture. Cerebral hæmorrhage is due to a conjunction in the brain of opposite vascular changes, the contrast between the thickened and toughened condition of some parts of

<sup>\* &#</sup>x27;Clin. Soc. Trans.,' 1878, vol. xi.

the vessels, and their thinned, bulging, and brittle wall in other parts, being most conspicuous in this organ. Hæmorrhage usually occurs late in cases of gout, and, as pointed out by Dr. Southey, after the degenerative changes leading to dilatation have begun in the hypertrophied myocardium.\*

In a series of thirty-two cases of cerebral hæmorrhage, Norman Moore found uratic deposits in thirteen, the ages of the subjects varying from twenty-eight to sixty-six.†

The Senile Pulmonary Hamorrhage of Arthritic Constitutions.—Of great pathological interest and clinical importance is the sometimes profuse hæmoptysis apt to occur, although rarely, in somewhat advanced life, not traceable to any causes but emphysema, and a gouty tendency either declared or latent. This remarkable affection was first described by Sir Andrew Clark, and little need be added to his masterly sketch. The writer has observed precisely the conditions described in an elderly female patient, in whom gout had never come to the stage of arthritis, but the gouty tendency was manifested in a variety of smaller symptoms. It must be inferred that the vascular condition is one of weakness, probably connected with changes in the pulmonary artery identical with the atheroma almost constantly found in the systemic arteries of gouty subjects.

# THE LYMPHATICS, AND GOUTY LYMPHANGITIS.

That the lymphatic system must be inseparably connected with the pathology of gout is almost a truism. There is, however, little outward evidence of its participation in the morbid events. The absence of any coarse changes in the glands and in the larger vessels does not, however, exclude the probability of intimate changes in the

<sup>\*</sup> Cf. Duckworth, loc. cit., p. 109. † Ibid. † 'Med. Soc. Trans.,' vol. xiii., 1890, p. 9.

chemical composition and in the cellular structure of their contents. There is in this direction a wide field open for future investigation. On the other hand, an occasional implication of the peripheral lymphatics belongs to the best-known clinical phenomena of gouty inflammation, and in connection with them reference will be made to the combination of lymphangitis with phlebitis in phlegmasia alba dolens.

Gouty Lymphangitis.—Whether the acute attack of gout may be regarded or not as intimately bound up with inflammation of the lymphatics of the part, or whether phlebitis has a larger share in the production of the œdema, is a question which needs for its solution further clinical observation. To say nothing of the strong analogy, with differences, presented by the acute rheumatic joint affection, in which the lymphatic implication is unquestionable, various features belong to the acute gouty swelling which remind us of the results of acute irritation of lymphatic capillaries. On the other hand, there is no evidence that lymphangitis of the larger trunks forms part of the process.

Gouty lymphangitis itself is apt to occur entirely independently of the arthritic seizure; but its gouty nature is attested by unmistakable evidence in some cases. other times it is doubtful whether it had been set up spontaneously, as seems to be the case with gouty phlebitis, or as a result of some unnoticed cutaneous lesion.

Gouty lymphangitis may occur in connection with ulceration of tophi. Erysipelas or gangrene has repeatedly been observed after surgical interference with the deposits, and this liability strongly discourages their removal by the knife.

The course of the affection is not different from that of ordinary lymphangitis. Suppuration may occur, or, in severe cases, diffuse inflammation and sloughing.

# CHAPTER XVII.

# THE VISCERAL LESIONS IN GOUT.\*

## THE MUCOUS MEMBRANES.

WITH the exception of the lining membrane of the upper respiratory tract, the mucous membranes are not favourably situated for a study of the gouty changes. From analogy, and from a study of the symptoms, we may infer that vascular and vaso-motor changes analogous to those to be described later in the pharynx, may be set up in the stomach and intestine. But concerning these questions our attitude is one of reserve until some further light is obtained. With the exception of an instance recorded by De Mussy,† in which the pharyngeal follicles discharged carbonate and urate of lime, and of Hayem's unique observation of a fine uratic incrustation of the intestinal villi,‡ mucous membranes have not been suspected of any liability to uratic deposits; but here again further search is indicated.

# GOUTY LARYNGITIS, TRACHEITIS, AND BRONCHITIS.

The mucous membrane of the respiratory tract is, in this country, exceedingly prone to suffer in those who are

<sup>\*</sup> Additional data concerning organs not mentioned here will be found in the clinical and pathological sections.

<sup>†</sup> Union Méd., xviii., 1856.

<sup>‡</sup> Rendu, loc. cit., p. 40.

gouty, and we have been led to speak of the conditions as 'gouty laryngitis, tracheitis, and bronchitis.' Uratic deposits, on the other hand, are rare in any part of the respiratory system, but especially rare in the lung itselfthe least unusual site being the larynx, and the air-passages being also liable in a feeble proportion. Thus, Bence Jones has described gouty deposits in the bronchial wall. The uratic expectoration described by various authors might conceivably have had the same derivation; but, with greater probability, it was due to the ulceration of laryngeal tophi. Gouty deposits in the larynx have been reported from time to time by reliable observers, including Virchow and Sir A. Garrod. Their situation has generally been the vocal cords or the cartilages. These facts are in complete harmony with the extensive clinical evidence pointing to gouty irritation of the laryngeal mucous membrane.

Gouty bronchitis occupies a larger place in the clinical history of gout—in connection with which it will be described—than in its morbid anatomy. It probably is in a great measure, though not wholly, answerable for the frequency of emphysema. Pleural adhesions, chronic interstitial and pneumonic changes, associated with dilated bronchi, are not infrequently seen.

Pulmonary tuberculosis is unusual in the gouty, except in profound cachexia, but not unusual in their offspring.

#### GOUTY EMPHYSEMA.

The prevailing anatomical pulmonary lesion in gout is emphysema, as bronchitis is the prevailing clinical ailment. It would seem, however, that chronic bronchial catarrh and the mechanical stress of cough are not necessarily forerunners of the change. Dr. Norman Moore has found

emphysema in so large a proportion of cases of inveterate gout that the numbers must include many cases in which bronchitis could not have been alleged as a sufficient cause. He is inclined to regard emphysema as hardly less frequent in gout than interstitial nephritis. This view entirely agrees with the estimate which is taken of gout in these pages. The pulmonary atrophy is part of the general malnutrition of the tissues, and the change is specially marked because the lung is essentially a part of the vascular system, and therefore subject in a high degree to the influences arising from the blood; and it is probably also connected with the enormous extent of the delicate and perishable capillary system, and with the high proportion of the elastic and fibrous elements in the pulmonary structure-both elements being known for the slowness of their nutritive changes, and one of them at least (the fibrous) being undoubtedly obnoxious to gout.

The frequency of emphysema has much clinical significance of a general kind, and especially in connection with pulmonary hæmorrhage, the occasional occurrence of which has been pointed out.

## THE KIDNEY.

The 'gouty kidney' is the small granular kidney described by Todd, George Johnson, Dickinson, Garrod, Charcot, Cornil, and others. Thickening of the capsule, shrinking of the organ, and granulation of its surface with cortical atrophy, are the well-known characteristics of the disease. On section, an almost fibrous toughness and a fleshy redness are described by Dickinson as belonging to the gouty kidney, though not exclusively to this. An additional feature, which may identify the granular kidney as a 'gouty' granular kidney, is the occasional presence of deposits of sodium biurate, whether within the col-

lecting tubes (Charcot, Cornil) or in the chronic inflammatory interstitial substance (Garrod, Rendu). Ebstein points out that gouty subjects sometimes present a granular kidney quite free from any uratic deposit, and that, especially in those who have previously suffered from gravel, uric acid may be found instead of biurate. According to Duckworth, deposits are rarely found in the kidneys of the gouty. Might this not be the result of the solvent treatment, or even of the diuresis special to granular kidney?

Whether it be complicated with deposits or free from them, granular kidney is usually regarded as a late result of gout. It is most often found in those whose gouty record is of long duration, and Dickinson\* ascribes to the enduring nature of the cause the fact that the gouty kidney commonly advances to the most extreme degeneration compatible with life. Granular disease being one of slow progression, it is difficult to estimate the date of its earliest beginnings. Levison has recently sought to identify it with that of the early gouty symptoms, a somewhat extreme view, which has been combated by Lange, but which is not entirely novel. Virchow long ago expressed a notion that a gouty nephritis might exist without either classical gout or uratic deposits, and Duckworth is inclined to admit the possibility of a 'primary gout in the kidneys.' Complete evidence as to the gout having been primary in the kidney is, however, difficult to secure, since a quiet gout in the joints is of common occurrence, whilst, on the other hand, uratic deposits may be reabsorbed in the course of time from joints previously affected.

Again, Lancereaux+ has described in chronic rheumatic arthritis a variety of granular kidney consecutive to chronic alterations in the arterial system; in other

<sup>\*</sup> Loc. cit., p. 157. † Cf. Duckworth, loc. cit., p. 100.

words, an arterio-sclerotic form, which might simulate the strictly gouty variety.

The Relative Frequency of Granular Kidney in Gout.—
On this important question Sir Dyce Duckworth\* has collected evidence. Ord and Greenfield† found, among the hospital cases in which the great toe was affected, a definite co-existence of contracted granular kidney in two-thirds, and in the remaining one-third renal conditions closely allied to the latter. In 96 cases of renal disease there were at least 8, and probably 9, in which no uratic deposits were found in the joints.

Dr. Norman Moore, in 49 cases of chronic interstitial nephritis in males, found uratic deposits in 22; in 16 females they were present in 5 cases.

Dickinson's 69 fatal cases of granular kidney included 16 cases of gout. It is to be observed, however, that the joints in this series were not examined.

The Situation of the Renal Deposit.—Opinions are divided as to whether the depositions originally take place in the tubules or in the intertubal tissue. According to Garrod, who holds that acute gout sometimes attacks the renal fibrous tissue before the joints, setting up acute pain in the loins, and temporary albuminuria, 'the greater part is interstitial, whereas in non-gouty cases the tubular structure is specially affected, and the crystals of uric acid and biurate are larger, though far less widely distributed.' The same view is shared by Charcot and others.

Cornil and Ranvier state that the urates are primarily in the cells which are the centres of their crystallization; Senator says that the amorphous salt is first deposited in the tubular epithelium, thence extending into the

<sup>\*</sup> Loc. cit., p. 100.

<sup>† &#</sup>x27;Transactions of the International Medical Congress,' London, 1881, p. 107.

interstitial tissue and becoming crystalline; Greenfield has commonly found the deposit in the connective tissue of the cortex, but rarely in the tubules; and Norman Moore, in 80 cases of well-marked gouty arthritis, found deposits in the pyramids in 6 cases, in the tubules in 6 cases; thus, hardly one-seventh of the number had either tubal or interstitial deposits. Sir Dyce Duckworth,\* who quotes these authorities, does not favour the idea that gouty kidney depends on the deposit, or, at any rate, is constantly associated with it. He also refers, in connection with the deposition of uratic salts, to Paget's observation that in children of the middle and upper classes, in whom inheritance of the diathesis may be expected, calculus of any kind is one of the very rarest diseases. We should bear in mind that the 'classes' form a much smaller aggregate than the 'masses,' and that in children of the poor lithates are the most common constituents of stone. Klebs observes that urates are deposited in the pyramidal tubes in very young children, but 'never in those whose lungs are unexpanded.' Lastly, Fagge notices that 'uratic deposits in the kidney are common in Germany; gout rare.'

The early and transient renal changes, the existence of which is assumed by the supporters of the renal theory of gout, need not be of the same order as those ultimately leading to the 'gouty granular atrophy.' The fact that many sufferers from acute gout preserve to the last perfectly healthy kidneys points to the opposite conclusion. The opportunity of ascertaining what these lesions may be, if they exist, occurs but rarely, as a result of sudden or accidental death, and is yet more rarely utilized; for the present they must remain matter of speculation, although their reality is stoutly asserted by Levison.

<sup>\*</sup> Loc. cit., p. 103.

## THE LIVER.

In spite of a full recognition of the importance of the liver in relation to gout, no organic disease of the liver. has been discovered by modern research. Hepatic cirrhosis. has not been made out, as in the case of renal cirrhosis, to be directly traceable to this affection. Murchison, Trousseau, Gairdner, Ebstein, and others, whose inquiries have been specially directed to this point, have found little evidence of its occurrence; whilst Dr. Norman Moore's tables teach us, as we were prepared to learn, that hepatic cirrhosis most commonly occurs quite independently of any uratic articular deposits. Sir Dyce Duckworth,\* who refers to these authorities, whilst recognising that much hepatic disease is strictly referable to disturbance of the circulatory system, still inclines to the view that true cirrhosis may be induced by gout. At the same time he admits fully the difficulty in proving this position. Dr. Robson Roose draws attention to the facts that gouty cirrhosis had been described by Trousseau, and that Budd also held that various substances besides alcohol might excite perihepatitis, and that the cow and the pig are subject to a hepatic cirrhosis obviously not alcoholic.

The broad conclusion is manifest that cirrhosis of the liver is not among the usual results of gout. Even the minor evil of cholelithiasis cannot be regarded as specially belonging to, although frequently observed in, gout.

With the exception of the chronic changes secondary to pulmonary or cardiac disease, we are not familiar with any other naked-eye lesions, and their absence, in itself, renders improbable the existence of any minute textural changes in the organ. Nevertheless, the prominence of

<sup>\*</sup> Loc. cit., p. 110.

the hepatic symptoms in the clinical history of the disease warrants the assumption of functional disturbances in the portal and in the biliary circulation, the evidence of which is more readily supplied by clinical than by anatomical investigation. We are also justified in suspecting that the hepatic metabolism is liable in gout to profound alterations, which need not, however, be bound up with obvious changes in the intimate structure.

Biliary Lithiasis.—The frequency of this complication is variously estimated by different observers. Dr. N. Moore found only three cases of biliary calculi in eighty cases of gout. Sir Dyce Duckworth, however, regards biliary lithiasis as not infrequent in gouty families. Renal and biliary calculi not infrequently coincide. He also observes that gallstones are somewhat rare after fifty, and also rare in hot climates.

# THE NERVOUS SYSTEM.

Even less than in the case of the kidney or of the liver can it be said of the nervous system that its morbid anatomy justifies the position which has been allotted to it in the ætiology, or that to which it is entitled in the symptomatology of gout. Apart from the coarse lesions resulting from atheroma and hæmorrhage, to which reference is made under the heading of the vascular system, hardly any change has been discovered in explanation of the varied, and often severe, clinical events. Even diabetes, which, after apoplexy, is the worst nervous disorder in gout, possesses no morbid anatomy.

Uratic deposit is rare in any situation, yet it has been observed in the meninges in a few instances: by Cornil in the cerebro-spinal fluid; by Albert and Ollivier on the

spinal meninges (in one case the lightning pains of tabes had been diagnosed by Ollivier); by Charcot in the subarachnoid fluid in a gouty woman.

Duckworth admits that a gouty paraplegia may sometimes occur as a sudden metastasis from a joint, and that, although it may be complete and sphincterial, some cases may recover. Sometimes the attack would precede the gouty seizures.

Practically speaking, Musgrave's classification of the gouty paralyses and nervous affections (apoplexia, paralysis, vertigo, etc., arthritica) has remained unsupported by anatomical proof. Nevertheless, Sir Willoughby Wade has lately revived Graves' opinion that gouty inflammation of nerves and of the neurilemma might spread up to the cord, producing softening and various 'gouty paralyses.'

A gouty neuritis has been described by Dr. Buzzard, who strongly urges that sodium biurate may crystallize in the lymph sheaths of nerves, and thus set up the motor, sensory, and vasomotor symptoms, and the neuralgiæ, so common in gout, and which Graves had long since attributed to perineuritis. As a working theory in explanation of the clinical nervous phenomena, this view possesses practical importance.

#### THE MUSCLES.

The muscular system is not largely involved in the clinical history of gout, although rather closely concerned in its general ætiology. We are not acquainted with any gouty alterations in muscular tissue, though uric acid has been found as a deposit within it in exceptional cases, and in particular in the myocardium. The uratic infiltration of tendons in the vicinity of joints has been already described.

# THE PATHOLOGY OF GOUT.

# CHAPTER XVIII.

# URIC ACID, THE LIVER, THE KIDNEY, AND THE NERVOUS SYSTEM.

URIC ACID IN RELATION TO GOUT AND TO ITS LOCAL PHENOMENA.

Since the prominent place occupied by uric acid in the morbid anatomy of the coarse lesions of chronic gouty arthritis and tophi, and, in a less degree, of acute gouty arthritis, has been fully recognised, a similar claim has been set up in favour of its connection with the pathology of gout itself, but with much less foundation in fact.

Because uric acid is invariably present in the main lesions of gout, and at times present in excess in the blood, and because it is apt to accumulate in enormous quantities in tophi, we should not hastily take it for granted that it is the essential or the only gouty product. Its insolubility and tendency to deposition bring it before our notice; but it is, after all, but one product in a complicated chain of metabolism. Its production is bound up with that of many other substances of which we have taken little account, and the relative value of which we have not determined, and also with important modifications of the tissues,

if there is any truth in the view that it is partly a product of the disintegration of the latter.

Concerning the local manifestations connected with a deposit of uric acid we know much-thanks to Sir A. Garrod, and, more recently, to Sir W. Roberts-but we are very far from knowing all. We are still ignorant whether the uratic deposits are entirely imported into the joints or in part produced there; whether they occur in absolutely healthy cartilage, or only after previous damage or disease; whether the deposition is always preceded by a degenerative or ulcerative process, as suggested by Ebstein; or whether it is not rather the cause of the irregularly pitted or excavated surface of the cartilage. We have no absolute evidence that in acute arthritis the acicular deposit is the cause of the pain and of the inflammation; much evidence tends in another direction. We are not sure to what extent, as suggested by Garrod, and previously by Sydenham, the articular attack may use up any previous deposit, and thus act in a curative manner. These are some of our present doubts; and they concern the local aspect of gout, which is by far the easiest of approach.

Constitutional gout is a much more difficult question; and it must be confessed that here we possess nothing more than theories.

- 1. The first view is that excess of uric acid is the essence of gout, and that the excess is derived from nitrogenous food.
- 2. According to another view, uric acid, howsoever produced, is not necessarily the essence of constitutional gout, yet it acts as the cause of the gouty attack.
- 3. A third view regards uric acid as resulting from the acute gouty arthritis, or, where this has not occurred, from some analogous process.

4. Lastly, there is the view that it is a by-product of the intimate changes which constitute gout; and that the results connected with its deposition are, to a great extent, mechanical, and strictly separate from the original pathological cause of gout.

The first must be characterized as an extreme view, evolved from large assumptions, which would need to be carefully examined before acceptance. The second and third are open in part to the same objection, but they share with the first a facility for explaining the temporary outbursts of gout in those whose intervening health is apparently normal. The last view is that most in harmony with the notion that gout is a disease of the entire organism, and that its local manifestations are governed by localizing circumstances or individual peculiarities of tissue.

We still hesitate, then, to admit, without further investigation, that gout is primarily dependent upon uric acid as a cause, or that uric acid necessarily exerts any exclusive influence in the production of the phenomena of goutiness.

#### THE RENAL THEORY.

Among the great pathological problems of gout, one of the most puzzling is the behaviour of the kidney. Has it an active part in the production of the disease, or does it only feel its effects? Two circumstances have deprived us of an easy answer: our ignorance as to the part played in health by the kidney in connection with uric acid production and excretion, and the rarity of opportunities of studying the pathological anatomy of the kidney immediately before, during, and immediately after the attack. We have been hitherto dependent upon inferences, and these may be classified as anatomical and clinical.

I. Destructive changes of greater or less extent are the

rule in chronic gout, as elsewhere dwelt upon. It is, however, a fact of primary significance that the rule is not
absolute. According to Sir Dyce Duckworth,\* 'It is
certain that gout may occur in the ordinary articular form
without implicating the kidneys, which may remain sound
even in old age. In such cases there is usually a fine
constitution, great resistance, and vigour of the tissues,
and the progress of the disease is kept at bay and overcome by the vital organs.' In primary renal gout the
general health is poor, and a progressive cachexy works
its special ravages, ending life prematurely.

A single case of immunity from renal disease would be enough to prove that renal disease is not a sine qua non for the production of gout.

From the other side of the question arises still stronger evidence—gout is not among the common results of extensive destruction of the kidney. The field of observation in this case is singularly extensive. It need hardly be pointed out that the results of experimental destruction of the kidney in healthy animals (Zalesky, Ebstein, and others) cannot be adduced as elements of proof in connection with human gout. Anatomical evidence thus favours the conclusion that kidney disease is not responsible for the causation of gout.

2. Precisely similar inferences are the outcome of clinical experience. Sir A. Garrod's original observations on the urine (loc. cit., p. 133) showed, besides a relative diminution in the bulk of the fluid, that during the early stage of an attack there was a diminution in the output of uric acid (to be followed by an increase as the attack passed off, sufficient in some cases to be regarded as a critical discharge), whilst the amount of urea remained at a fair average. Slight albuminuria may also occur, but it is not

<sup>\*</sup> Loc. cit., p. 101.

common in the first attacks. With the sole exception, therefore, of concentrated urine, and of an ephemeral diminution of uric acid, the renal function is normal, and may, under favourable circumstances, remain normal through life subsequently. Sir A. Garrod's theory of the causation of the attack being based on this single deviation, it is right to mention that other observers, in particular Lecorché, have failed to find any diminution in the amount of urine secreted, or in the quantity of uric acid, both of which are stated to have been increased in some cases.

The objection that the diminished uric acid excretion is not constant in gout, is met by the statement that the percentage is a widely fluctuating one in health. The elaborate examinations of L. Vogel point to diminished excretion.\* Vogel, in three cases of more or less chronic gout with exacerbations, in which food, urine, and fæces were examined, found a remarkable nitrogen retention, much in excess of that belonging to the uric acid retention. The patients behaved in this respect like sufferers from renal disease, although the clinical signs of granular kidney were wanting.

Absolute retention of uric acid has never been alleged; but with excessive production from any cause, the filtering apparatus may be rendered incompetent, and, the normal amount being excreted, there may be retention of the excess. In other cases renal inadequacy may be so great as to accumulate uric acid in the blood, in spite of a diminished production.

Levison† is the most advanced supporter of the theory of renal inadequacy. He maintains that gout cannot be developed without a primary renal lesion, which is almost

<sup>\*</sup> Zeitsch. für Klin. Med., xxiv., p. 512. Quoted by Dr. Archibald Garrod. Cf. Practitioner, July, 1895.

<sup>†</sup> Quoted by Dr. Archibald Garrod, loc. cit.

invariably interstitial. Almost every autopsy on a gouty patient has revealed some degree of lesion; the exceptions he professes to explain. In a series of forty-two cases of renal disease, examinations were made of the great toe and other joints. In twelve, uratic deposits were found, and in all of them some degree of granular kidney disease, whereas in thirty cases of other renal diseases no trace of uratic deposit was detected. He believes that in most instances the renal change long preceded the gout.

Levison places the earliest change in granular kidney in the epithelium of the convoluted tubes, the interstitial change being secondary, and he quotes Oliver and others as to the effect of lead. It has been shown that in granular atrophy the uric acid excretion is diminished, and there is an accumulation in the blood. Levison points out that albuminuria is not constant in granular kidney, so that the absence of clinical signs during years of apparent health may not necessarily imply integrity of the organ.

Into an examination of these conflicting statements it is impossible to enter. The alleged temporary disturbance of function is not without analogies. Functional albuminuria is a type of temporary abnormality entirely independent of organic disease. It would be rash, however, to state that this disturbance was mainly seated in the kidney; the conditions under which the albumen is held in the blood probably have the greater share in the result.

That the kidney must suffer some early disturbance from the gouty principles ripening for an outbreak is readily admitted: if gout has attacked one cell in the body it has attacked them all. At the same time, circumstances point to a preservation of the functional activity of the organ throughout the crisis. In cases of chronic gout the special implication of the kidney is easily accounted for. For years the renal epithelium has been overstrained in its most complex department of work—that of nitrogenous excretion—and in its most trying medium—the strongly acid medium; salts of uric acid have crystallized in the organ, and become irritating foreign bodies:—serious and varied are the evil consequences. All this, however, is but the late result of the gouty state of which we seek the cause, and can hardly be adduced as throwing light upon the latter.

More direct evidence is needed than has been hitherto supplied that the kidney is at fault in the first instance, although there is a pleasing simplicity and much likelihood in this way of explaining the altered proportions of uric acid in blood and in urine.

If dependent upon the kidney, it is remarkable that this failure of excretion should be limited to a single substance, and that it should so quickly be replaced in some instances by the opposite state of increased discharge. 'The acid is thrown out in much larger quantities as the disease is passing off, and amounts even above the patient's daily average may be excreted, forming the so-called critical discharges.'\* Again, in speaking of some cases of chronic gout, Garrod says,† 'It will be noticed that, although the quantity of urea remains nearly constant and normal, the uric acid is not only exceedingly deficient, but subject to the greatest fluctuations.'

Since in all these cases the blood contained, presumably in a permanent way, much uric acid, the alleged failure of the kidney would be a peculiarly fitful one, and in that respect unlike the behaviour of structural disease.

We are also struck by the fact that, whilst no morbid change may be detected in the kidney, structural changes are going on elsewhere—in the joints and in other parts affected—which we must admit as evidence of unseen

<sup>\*</sup> Garrod, loc. cit., p. 133.

<sup>†</sup> Loc. cit., p. 141.

changes taking place in the blood. We are tempted to correlate the disturbed function rather with these manifest changes than with an organ apparently healthy, fulfilling in other respects its normal functions, and to ask whether the uric acid may not be rather held back in the blood than refused passage through the kidney. Both suppositions entail subtle influences difficult to explain.

Adopting the statement of Sir A. Garrod, we still are left to infer that the original renal disablement is partial only and evanescent, and we must conclude that the organic affection, if present, is exceedingly slight.

An absolute demonstration that an increase of uric acid in the blood and its diminution in the urine are strictly simultaneous events would remove a possible source of fallacy. If the quantity of uric acid circulating in the blood is capable of variations as rapid as those suggested by Dr. Haig's observations, the want of agreement in the proportion of uric acid in the blood and of that in the urine might be more apparent than real. Sir A. Garrod's observations appear to be free from any suspicion of errors of this kind.

Sir W. Roberts provides us with an ingenious suggestion as to the possible nature of the renal defect.

'The presence of uric acid in mammalian urine might be regarded as a vestigial phenomenon,' evolution having gradually replaced uric acid by urea, and proportionately educated the urea-secreting function, whilst the uric-acid-secreting function was progressively undergoing obsolescence. Residuary features being very apt to vary in individuals, some of the liability to gout might be explained by an unduly marked involution of the function last named. Again, the two functions being complementary, family gout might have its origin in the overworked state of the urea-secreting function in the goutily

inclined (who are generally hearty partakers of meat, and therefore produce much urea as well as some uric acid—as I to 15—in excess of the normal). 'There would thus arise a persistent demand on the urea-excreting faculty, which could only be satisfied by an encroachment on the residuary faculty for the excretion of uric acid.'\*

This brilliant attempt to bring gout, as it were, within the scheme of Darwinism implies also a recognition of the paramount influence of individual susceptibility, considered in this case in connection with the kidney.

If without uric acid there is no gout, the way in which the accumulation takes place in the blood is more than a pathological problem: it is a practical one. Sir W. Roberts does not pretend to offer more than suggestions on this point, believing in a restricted renal capacity for uric acid excretion in the race, and in a special restriction in some individuals. Accumulation would, according to him, begin with the overtaxing of the kidney with nitrogenous excretion. The varying factor is thus the degree of overwork of the kidney; slowly the arrears of uric acid would creep up till extensive accumulations might be brought about.

The chemical history of the phenomena of gout as told by Sir W. Roberts constitutes a complete, a consistent, and an adequate theory, which possesses over all others the advantage of being based upon facts readily demonstrated in the laboratory. These facts are a great and permanent addition to our knowledge of the subject. They shift the range of all future investigations to a higher level, and give them a novel and more definite direction. Indeed, if the conclusions to which they lead could be applied as rigidly to the case of living subjects as they are applicable to the chemicals used in the test-tube, we might regard the problem of gout as completely solved. At

<sup>\*</sup> Loc. cit., p. 120.

present this would be too sanguine a view. Their discoverer is the first to acknowledge that these conclusions cannot at present be transferred to clinical ground without some reservations. The conditions within the human body have none of that simplicity which lessens the great difficulty attaching even to a purely chemical investigation of the reactions of uric acid and of its compounds. Many factors difficult to control are known to interfere; and we cannot feel certain that additional factors hitherto unsuspected may not swell their number.

To what extent the chemical laws so admirably demonstrated by Sir W. Roberts may work true in the midst of the innumerable reactions complicating those in which the relatively small proportion of circulating uric acid is immediately concerned, is in itself a matter for speculation.

In conclusion, we must recognise that in the result the kidney is inadequate to the circumstances; nevertheless, the change may be in the circumstances rather than in the kidney.

We still need a proof that the kidney is primarily at fault. After all, the kidney is but the door out of the house, a humble function compared with the multifarious activities astir within. May not the uric acid, instead of being in the ordinary sense locked in, be detained or attracted by serum or cells, just as a powerful magnet placed in the centre of a stream might withhold metallic particles from the influence of the current which hitherto had over them an undivided control?

#### THE LIVER IN GOUT.

If gout can be correctly viewed as a disease of nutrition (and its intimate connection with the alimentary function none would doubt), the liver must have a place in its evolution. The clinical importance attaching to hepatic disorders is well known, in spite of the meagre data furnished by pathology. Whilst it is no less free than the kidney from any pre-existing structural disease capable of originating gout, we have various reasons for suspecting that the liver may take a large share in the manufacture of the affection; they are all connected with its activity as the great central chemical workshop of the organism.

The Ætiological Place of the Liver in Gout.—To say that the liver is concerned in the production of gout is, in a certain sense, a safe proposition. Its varied functions cannot all be entirely foreign to the disturbance. To allege that it was mainly at fault in the mode of disposing of the nitrogenous surplus would be to ignore other functional defects of equal importance. Some solidarity must exist between the various activities of the hepatic cell, and their joint implication is almost inevitable.

The precise position occupied by the liver in the ætiology of gout must remain doubtful, in connection with the extent of the physiological hepatic duties, with the remarkable tolerance of the organ in some directions, and with its multiple opportunities of going wrong. Again, for long periods its failures and shortcomings may remain latent. They neither affect structure, nor do they necessarily lead to perceptible changes in aspect; but meanwhile they may be reflected in states of the system.

By the side of these latent, invisible hepatic delinquencies, there are those which are more obvious. In a given proportion of gouty patients, we are struck by the hepatic or bilious look, and we are led to inquire whether in them the liver may not be the prime offender. If in them, may it not also exercise in others an ætiological influence not less real, though less manifest?

We are reminded that gout affects all constitutions, and among them the bilious, in whom a due proportion is at times lost between the secretion, the excretion, and the reabsorption of bile, and who are often, moreover, the subjects of functional nervous disturbances or nervestorms. It is more than probable that the hepatic inadequacy is not in them limited to the biliary function, but extends to other aspects of hepatic metabolism. Again, Murchison's lithæmia may obtain in those whose biliary function is not obviously at fault. It is idle, however, in view of the prevalent freedom of gouty subjects from biliousness and from lithæmia, to attempt to generalize from the peculiarities of these limited classes, and to refer the ætiology of gout to antecedent hepatic defect. We must be content to infer that the liver may take in the general nutritional changes which are probably bound up with goutiness, a share commensurate with its leading position in normal metabolism.

#### THE NERVOUS SYSTEM IN GOUT.

The Influence of the Nervous System in the Production of Gout.—The nervous system takes a leading share in the history of gout, and in the mechanism of many of its visceral irregularities; but as soon as we attempt to formulate its status as a supposed primary cause, we discover the vicious circle of the argument. We are thwarted at starting for want of working material. Of anatomical evidence the lack is absolute. The clinical supply is abundant, but of the wrong kind, intangible, imponderable, and useless for accurate inference or deduction. Until some independent alteration in the nervous centres can be demonstrated, we must regard them as also suffering with the rest from the pervading perversion of nutrition.

Their directing power in the causation of gouty phenomena is borrowed. Behind them is the real cause, which from its ubiquitous action throughout the system we are bound to identify with the juices. At the present stage, we still are unable to construct a nervous theory of gout on strictly pathological lines. We are restricted to the observation and to the discussion of the nervous phenomena witnessed in the gouty, and the range of our disquisitions is exclusively clinical.

# CHAPTER XIX.

# THE MORBID AFFINITIES OF GOUT.

# GOUT AND RHEUMATISM.

WE cannot fail to learn from a critical comparison between the two affections, the symptoms of which are so familiar and the causes so obscure.

Ætiologically they belong to different ages. In the young, articular rheumatism, so long overlooked, is now recognised as common, and as capable of varied manifestations. In old age it is rare.

Gout is decidedly uncommon before middle age, though sometimes seen as early as twenty, and exceptionally in childhood.

In common the two diseases possess the feature of heredity, though this is more prominent in gout than in rheumatism. In rheumatism, Sir A. Garrod found a hereditary predisposition in about 25 per cent.; Fuller in 27 per cent.; Chomel in 33 per cent.; and Dr. Archibald Garrod in from 30 to 35 per cent. In gout more than 50 per cent. of Sir A. Garrod's cases gave a hereditary history.

It is well known that in the individual an early liability to attacks of rheumatism is often followed by a gouty old age. Again, in both cases a first attack does not protect the subject, but strongly predisposes to a recurrence. In this country both diseases are largely prevalent; but the same parallelism is not found elsewhere. In both there is a disproportion between the sexes, in favour of frequency in the male; but the two diseases present a striking difference, gout being, according to Fagge and Pye Smith, eight or nine times more frequent in men than in women, whereas the Collective Investigation Committee\* found among 654 cases 375 males and 279 females.

Pathology.—Whilst our ignorance as to the nature of the poison of rheumatic fever is almost absolute, we know that in gout uric acid is in excess. Whether the theory which regards lactic acid as the rheumatic poison be ultimately proved correct or not, we recognise in rheumatic fever a greater resistance to the alkalizing effect of alkalies than in average subjects of gout, and a greater over-production of acid. Dr. Haig does not hesitate to pronounce this to be uric acid; and he adduces arguments in favour of a conclusion that rheumatic fever and gout are different utterances of one and the same malady, or at any rate diverging results from the same cause. Some of the reasons for withholding assent from this view will be given presently.

Clinical Pathology.—The clinical features of the two diseases present striking differences. The joint affection in rheumatism is typically polyarticular, in gout at first monarticular. The chronic attenuations of gouty arthritis tend to become more and more generalized in the body; those of rheumatism to be more and more localized.

In both diseases the agencies which determine the implication of the several joints are obscure, though not equally so. When, in a bed-ridden acute rheumatic case, the pain is transferred from the right knee to the left elbow, or to any other joint, we cannot successfully argue that the locality of the metastasis has been deter-

<sup>\*</sup> Brit. Med. Journ., February 25, 1888.

mined by any external influence. In the local incidence of gout very definite factors may often be found. Above all, there is the unaccountable but systematic regularity with which, in the large majority of cases, the great toe is attacked first. In exceptional instances this rule is departed from, and the influence of localizing causes may be demonstrated.

Thus, in a man confined to his bed with hemiplegia, the leg recovering quickly and the arm remaining paralyzed, gout may develop in the paralyzed hand. Again, local injury to a joint will often determine a gouty attack in that joint. In both these apparently opposite instances it is impossible not to trace a nervous influence, though views may differ as to the exact relation which this bears to the local mischief. Sydenham's classical observations on the efficacy of study in promoting a return of his gouty troubles supply another example of the connection to be traced between nervous agencies and gout.

In rheumatism, though the most used joint, or the injured joint, may sometimes suffer first, and though nervous fatigue may predispose, nothing comparable to the reactions described can be said to occur.

The joints affected present a very different history. In all uncomplicated cases acute rheumatism passes away and leaves the joint absolutely unchanged. With gout the restitutio ad integrum is apparent only; the cartilage bears a lasting trace of the specific inflammation. To this all-important distinction we shall presently revert.

The blood, which has been shown by Dr. Archibald Garrod to be so profoundly affected in rheumatism, presents no corresponding changes in gout.

The action of remedies, as at present employed, establishes a strong contrast between the two diseases. Although rare instances are recorded of the prompt disappearance and apparent cure of the acute gouty trouble, an abrupt cessation of the local inflammation is usually ominous of graver mischief about to arise elsewhere. In rheumatism we are now familiar with the rapid relief, under the influence of salicylates, of all the parts affected, without any recurrence in the other joints or any implication of the viscera.

Although this is but a fragmentary sketch of the features of likeness and of contrast of the two diseases, we may venture to draw from them provisional conclusions.

The differences are so great that, were they considered alone, the affections must be pronounced essentially dissimilar. Do the points of resemblance avail to modify this verdict? They do not argue much more than an identity in some of the structures involved. In both diseases the inflammation is thrown upon the joints and their fibrous surroundings; and in both the irritant is in great part extravascular and intralymphatic. A certain similarity must be expected in the reactions obtained from the self-same tissues, even when arising from irritations essentially distinct.

The dissimilarities existing between the irritating agents are not difficult to trace:

- I. In gout, a solid residue is almost invariably left by the attack; in rheumatism, nothing is left behind which even the microscope can detect, and during the seizure itself the anatomical changes are merely such as cells must undergo in any common severe inflammation. The irritant must be either a fluid, or, if a solid, one so subtle as to escape our present means of investigation.
- 2. The same conclusion is derived from the prevailing non-metastatic tendency of gout, and by the opposite tendency in rheumatism. The irritant in gout, though conveyed by the blood, is irritant only in its extravascular

phase. In rheumatism, whilst it is extravascular in its arthritic manifestations, the irritant circulates in an active state both in the lymphatic and in the blood stream. Hence gout leads to deposition within the cardiac wall; but rheumatism will profoundly affect the endocardial membrane and the blood itself, and rheumatic metastasis is probably but the expression of its ubiquitous presence within the latter.

Are Gout and Rheumatism capable of blending?—The question as to a possible association between gout and rheumatism has never been set at rest. There are still those who believe in an arthritic diathesis equally predisposing to either, the event being determined in each instance by the special circumstances of the attack. Charcot held this view; Dr. Haig is strongly of that opinion; and the same tendency of thought is expressed in Mr. J. Hutchinson's words\*: 'Gout is but rarely of pure breed, and often a complication of rheumatism. It so often mixes itself up with rheumatism, and the two in hereditary transmission become so intimately united, that it is a matter of considerable difficulty to ascertain how far rheumatism pure can go. . . . It is to this permanent modification of tissue that the peculiarities in the process (transitory rheumatic pains in joints, fasciæ, and muscles, chronic crippling arthritis, destructive arthritis with eburnation, lumbago, sciatica) are due.'

Clinically, this view seeks support in the fact that some gouty subjects not infrequently have suffered from acute rheumatic attacks. An opposite argument, however, might be based upon this. The tendency of rheumatism and the tendency of gout to recur being so great, the sudden appearance of genuine gout in one known to be rheumatic, instead of a rheumatic or even of a modified rheumatic

<sup>\* &#</sup>x27;Pedigree of Disease,' 1883, p. 126, quoted by Duckworth.

attack, goes far to suggest a radical difference between the two complaints, although in some of their symptoms they overlap, and in their imperfectly developed phases they may be difficult to diagnose.

## GOUT AND OSTEO-ARTHRITIS.

The relation between gout and rheumatoid arthritis is one of the most vexed questions of modern pathology. Its discussion cannot be attempted in these pages, and the reader must be referred for a complete study of the subject to Sir Dyce Duckworth's treatise on gout, and to Dr. Archibald Garrod's treatise on rheumatism. The writer's views may be expressed in a very few lines.

Of the existence of a disease entailing permanent articular damage and deformity, and essentially differing from gout and from rheumatism, sufficient evidence seems to be afforded both by the anatomical appearances and by the clinical phenomena.

Anatomically, its feature is a hyperplasia of cartilage, a change ultimately tending on the one hand to destructive softening, and to ossification on the other—and a hyperplasia of bone, a change tending to thickening and condensation of the bony constituents of the joints. In its extreme developments the disease would thus lead to the disappearance of a great part of the articular cartilage, and to an extensive formation and condensation of bone.

Inasmuch as each of these two concurrent changes may be variously active, different lesions and different types of disease will arise. All types, however (excluding only malum coxæ senile, which may be an altogether different affection), present well-marked features in common, the most striking of which is the symmetry of the lesion, a peculiarity alike foreign to rheumatism and to gout in its earlier manifestations.

Clinically, not this alone, but many other circumstances, support the view set forth by Dr. Ord, and largely entertained, that the affection is essentially conditioned by disturbed nerve agencies, whether viscero-reflex, or in connection with spinal or medullary centres or with an assumed trophic 'joint centre' in the vicinity of the vagus centre.

The disease affects individuals of widely different temperament and of various ages. The assumption of a prevailing nervous mechanism does not exclude the possible incidence of humoral influences. In the writer's opinion, based upon some observation, the disease may occur, and in younger women it often occurs, in a pure unmixed form, or it may affect those eminently rheumatic, or, lastly, those prone to gout or actually gouty. In practice he has met with 'simple rheumatoid arthritis,' with 'rheumatic rheumatoid arthritis,' and with 'gouty rheumatoid arthritis,' and the treatment has varied with the special form under observation.

Reverting now to the original question, the rheumatoid arthritis of the gouty may closely simulate genuine gout in its chronic form, which is often polyarticular, and may be symmetrical. Some of the lesions found in the one are apt to occur in the other. The lipping of rheumatoid arthritis may also occur in gouty joints. Heberden's nodules, so common in gout, were supposed by their discoverer to be limited to rheumatoid arthritis. The deformities due to the two diseases may present a considerable outward resemblance. The clinical history of the patient often fails to point to a distinction, so many gouty patients, especially women, presenting no acute monarticular seizure at the onset. It has often happened that cases have been mistaken, and this has added to the previous confusion.

In this country, where gout is so prevalent, not a few cases of rheumatoid arthritis are liable to gouty complications, partly, doubtless, under the influence of gouty heredity, which appears, though this point needs elucidation, to favour the advent of osteo-arthritis.

The coexistence with gouty deposits of changes resembling osteo-arthritis led Fuller\* and Hutchinson to believe in a blending of the rheumatoid with the gouty element—at least in some cases. This is the view also taken by the writer. Mixed forms may arise in which the osteo-arthritic changes are conspicuous, and uratic incrustations may also have occurred. This in no way invalidates the statement as to the independent character of the two diseases; indeed, their dualism always asserts itself either clinically or in their anatomical appearances.

# GOUT AND PHTHISIS.

Between the prevalence of rheumatism and of phthisis there is something more than the link established by the identity of the climatic factors, which in this country favours them both. Dr. James Edward Pollock† has given well-known proof of the frequency of this association.

The association with gout is much less often seen, nor was it to have been expected. Sir Dyce Duckworth‡ quotes the view held by Noël Guéneau de Mussy, that the arthritic and the tubercular constitutions are so far convertible as to be apt to alternate in their hereditary transmission, and that in the history of a gouty descendance the immunity of an intermediate, whilst not absolute as regards gout itself, might be tainted with marked tubercular or scrofulous manifestations. Sir James Paget's view is

<sup>\* &#</sup>x27;Rheumatism, Rheumatic Gout and Sciatica;' 1852.

<sup>† &#</sup>x27;Elements of Prognosis in Consumption;' London, 1865.

<sup>‡</sup> Loc. cit., p. 172.

also quoted, showing the intermixture in individuals by inheritance of the gouty and of the scrofulous constitution, each of which may assert itself, not only separately at the ages relatively obnoxious to each, but in combination with the other. Thus, the arthritis of gout may be modified by inherent scrofulous tendency, and assume a more chronic and destructive type. On the other hand, the phthisis of middle age, which, unlike the early scrofula of childhood, may come within the range of an active gouty influence, has long been known to be mitigated by the association in question. An arthritic or gouty form of phthisis was formerly described, and even Laycock recognised an 'arthritic tubercular cachexia.'

Sir Andrew Clark has shown that the senile cases characterized by copious hæmorrhage, by dyspnœa, by immoderate cough and expectoration, and by ultimate recovery when the hæmorrhage itself is not fatal, are not cases of phthisis, but of emphysema.\*

Putting aside such cases, evidence is found, as shown by Dr. Pollock, that in genuine phthisis the advent of gout is in a measure protective, and favours a chronic mild type. To this view Sir Dyce Duckworth adds his testimony, believing that the modifying effect of gout is perceptible in two directions:

- 1. In more than the usual tendency to initial and to recurrent hæmoptysis; and
- 2. In a marked tendency to cicatrization, in spite of gouty acerbations of the articular process.

He also reminds us of another well-known form of the association. The phthisis, which sometimes supervenes at a late stage of chronic gout, may benefit from the gouty hereditary influence which may still linger in the economy. But, in other cases, the existence of a pro-

found gouty cachexia may assist, at any rate does not materially delay, the destructive changes in the lung.

# GOUT AND CANCER.

The connection between gout and cancer needs further study. That the two diseases should frequently coincide is natural, as they are liabilities of the same period of life. Various writers have expressed their belief in a more direct relationship. Sir Dyce Duckworth, who has examined the evidence of this alleged connection, is not impressed with the existence of any proof of an arthritic predisposition to cancer.

# GOUT AND OBESITY.

The conjunction of these two names under one title is not meant to imply a necessary association or any intimate pathological connection between gout and obesity. So far from being identical, they only wear that 'family air' which strikes us most in brothers who happen to be in every line of feature most different. In spite of that lack of direct resemblance, kinship exists between the two affections, often plainly to be traced, though we should not attach too great an importance to this circumstance.

Reference has already been made to Scudamore's tables of frequency of obesity in the gouty. Bouchard\* has devoted special attention to the whole subject, which should be read in his interesting pages. In 94 cases, observed presumably in France, where gout is less common, Bouchard found gouty antecedents in 28, and rheumatic in 33. In a majority of the remainder of his cases migraine, diabetes, lithiasis (renal and biliary), eczema, and neuralgia gave evidence of an 'arthritic' habit.†

<sup>\* &#</sup>x27;Maladies par Ralentissement de la Nutrition.'

<sup>+</sup> Cf. Duckworth, loc. cit., p. 195.

Early obesity occurs in gouty families, rather commonly in the Hebrew race, and it is often associated with gravel.

Obesity with glycosuria is also a gouty conjunction, and the term 'fat diabetes' points to this connection. Duckworth states that occasionally fat diabetics gradually become lean diabetics, and he also notes that obesity may long precede glycosuria.

It is in the treatment and management of gout and of obesity that their resemblance stands out most clearly. These affections are primarily and essentially dietetic; their treatment is based upon retrenchment, for in both alike there is a surplus of nutrition. The gouty and the corpulent, not only in some aspects of their disease, but in the details of its cure, are apt to be fellow-sufferers.

It is unnecessary to dwell upon the other constitutional diseases. *Syphilis*, when it happens to complicate gout, gives rise to peculiarities in the clinical symptoms to which Mr. J. Hutchinson has invited further attention. The combination in question has not hitherto thrown fresh light upon the pathology of gout.

Struma is among the recognised kinship of gout. Charcot\* has shown that the several members of the same family may suffer individually from gout, scrofula, diabetes, and obesity. The relation between gout and struma in hereditary transmission is a matter of frequent observation in practice.

### GOUTY GLYCOSURIA, AND DIABETES.

The pathology of gouty diabetes and glycosuria is, if it were possible, even more puzzling than that of the uncomplicated conditions. The whole subject is at present

<sup>\* &#</sup>x27;Leçons sur les Maladies des Vieillards et les Maladies Chroniques, p. 98; Paris, 1868. Quoted by Duckworth.

an almost exclusively clinical study; nevertheless, like the equally obscure subject of lead-gout, it is fertile in suggestions.

We must forbear entering into clinical details, and merely state in the shape of propositions the recognised results of clinical experience:

- 1. The genuineness of a gouty connection in many cases of temporary glycosuria is proved beyond doubt; this is also true of some cases of diabetes.\*
- 2. The intermittent glycosuria of elderly and obese persons, which has been regarded as a simple result of digestive inadequacy, is more common in gouty subjects than in others, and in them is more prone to pass into a permanent diabetes. Diabetes originating *early* in life is sometimes observed in the descendants of gouty persons.
- 3. Diabetes originating late in gout is specially mild in type, slowly progressive, liable to fluctuations, and even compatible with longevity. A proportion of the sufferers are obese, many present for a time the florid complexion and full habit of relatively robust health. Neither the diuresis nor the wasting which characterize the progress of diabetes when due to other causes is a prominent feature of this variety. The daily amount of urine may hardly exceed a full normal average.
- 4. Gouty glycosuria often alternates in the individual with other visceral manifestations of gout, and particularly with the neuralgiæ and the visceral neuroses, and with gravel. Gravel sometimes coincides with the glycosuria;
- \* A historical review of the growth of our clinical knowledge on this point is given by Sir Dyce Duckworth (*loc. cit.*, p. 178), who quotes the opinions of Willis (1674), Trotter (1788), Stosch (1828), Naumann (1829), Prout (1843), Bence Jones (1853), Gairdner (1854), Claude Bernard (1855), Laycock (1862), Marchal de Calvi (1864), Charcot (1868), Garrod, Roberts, Dickinson, Ord, Brunton, Lecorché, Lancereaux, Lasègue, R. Schmitz, and others.

its absence in most of the cases may be explained as a result of the diuresis.

5. The same explanation has been applied by Garrod to the prevailing dissociation between the glycosuria and the articular attacks. With the exception of a slight and ephemeral glycosuria which may accompany acute gout, the appearance of sugar in the urine usually coincides with a remission of the gouty manifestations. This fact has probably suggested the belief formerly entertained in a direct antagonism between gout and diabetes.

Much pathological speculation has arisen from a consideration of these and of many other minor peculiarities of the affection under review. The intermittence of the glycosuria, and sometimes even of the diabetes, warrants at least one conclusion, viz., that, at any rate in its beginnings, gouty diabetes is a functional rather than an organic disorder. Opinions are almost unanimous in favour of the liver as the seat of the disturbance, but as to the mode of origin, and as to the mechanism of the latter, they diverge. From the standpoint of gout two views present most interest. The hepatic disorder is variously held to be primary, or to be induced by nervous agencies. supporters of both these theories are led by the well-known alternation between the glycosuric and the articular troubles to regard glycosuria as one of the manifestations of gout, as 'gout in the liver' in opposition to 'gout in the joints.' The study of gouty diabetes is thus shown to be another approach to the study of the pathology of gout. Whilst it affords arguments in favour of the neural hypothesis, it distinctly favours the theory that the liver is largely concerned in the production of gout, and chiefly by virtue of the leading part which it takes in the processes of metabolism and of nutrition.

## THE RELATION BETWEEN GOUT AND HÆMORRHAGIC DISEASES.

For a valuable study of these diseases Sir Dyce Duckworth's work should be consulted. Splenic leucocythæmia, in which the very large amount of uric acid excreted may give rise to renal calculus, does not lead to gout, and the two isolated cases reported\* must be regarded as exceptional. An isolated instance of purpura and one of paroxysmal hæmatinuria in gouty subjects are also recorded.

The chief interest attaches to hæmophilia. Its alleged gouty connection, contended for by Rieken as early as 1829, has been subsequently supported and opposed with equal vigour. Dr. Wickham Legg, in his valuable contribution to this subject, 'A Treatise on Hæmophilia' (1872), questions the correctness of Rieken's original propositions, which are as follows:

'I. The tendency to extreme hæmorrhages has been of late observed only in those whose parents or grand-parents have suffered from gout. 2. In those members of "bleeder" families who have escaped the tendency to hæmorrhage, gouty paroxysms may be observed. 3. In "bleeders" themselves gouty paroxysms are nearly always seen, and sometimes an alternation of the joint affection with the bleeding. 4. Gout is a disease which stands in a very close relation to the blood and bloodvessels, and often appears to be a direct cause of hæmorrhage.'

Sir Dyce Duckworth, whilst not adopting Rieken's extreme view that hæmophilia is an anomalous variety of gout, and the articular attacks practically gouty arthritis, adduces, nevertheless, strong evidence in favour of a

<sup>\*</sup> Cf. Duckworth, loc. cit., p. 198.

definite hereditary relationship between gout and hæmophilia, and of an association between them in respect of structural peculiarities. Jonathan Hutchinson holds that the vascular weakness is developed by gout and further specialized by serial hereditary transmission.

Sir Dyce Duckworth insists upon the striking parallelism shown by the two affections in the direction of the nervous system (including the occasional complication of epilepsy); in the direction of the joints; and in other directions also. He also notes the tendency to recurrence, which would support the view that the hæmorrhage of severe hæmophilia was that of a 'gradual accumulative plethora which must perforce discharge itself.' In this respect also an analogy would be traceable between the gouty and the hæmophilic groups.

#### CHAPTER XX.

#### PLUMBISM AND LEAD-GOUT.

#### THEIR INCIDENCE AND GENERAL ÆTIOLOGY.

IN 1854 Sir A. Garrod\* published the fact that 'at least one in four of his hospital patients suffering from gout had, at some period of their lives, been infected by lead, and for the most part had followed the occupation of plumbers or painters.' In the third edition of his work on gout† he refers to prior observations of this association by Musgrave, Huxham, William Falconer (1772), C. H. Parry‡ (1807), and Todd, and to the descriptive expressions 'lead arthralgia' or 'metallic rheumatism' used by Sauvages.

The frequency of the combination of lead intoxication and of gout among lead-workers in London has been confirmed by other observers, but the same frequency has not been noted in any other locality. Christison's original report bore witness to the total absence of lead-gout in Edinburgh, and at the same time to the infrequency of plumbism. This statement has subsequently received some qualification, but the fact remains that lead-gout is exceedingly uncommon, not only in Edinburgh, in the whole of Scotland, and in some of the Northern towns in

<sup>\* &#</sup>x27;Med. Chir. Trans.,' vol. xxxvi. † Loc. cit., p. 237.

<sup>‡</sup> It is significant that Parry attributed the effect of the metal to its power of 'producing arterial plethora.'

England, but in Ireland, in France, and on the Continent generally. This striking contrast, though it may seem at first sight likely only to complicate the problem of gout, really affords help towards its solution, provided we can define with sufficient accuracy the main differences between the London lead-workers and lead-workers throughout the world.

Had the occurrence of lead-gout been absolutely confined to London and other large towns in the South of England, and strictly excluded from the North and from Scotland, whilst all other factors were identical, important conclusions might have been framed. It would have been equally obvious that gout is not produced by lead per se, and that the operation of certain gout-producing causes, absent elsewhere, but present in England and London, is vastly assisted by it.

The statements originally made by Sir A. Garrod can still, in spite of any exceptions which have since been pointed out, be accepted as substantially correct, and as affording a fair basis for inferences; and if we may assume that the hours of labour, the degree of exposure, and the lesions due to lead, are fairly constant qualities, the remaining possible differences would relate mainly to race, climate, and diet.

All the varieties of the London climate are to be found in some one or other of the localities belonging to the opposite section. The towns of Scotland, Newcastle, and other towns in the North of England, the cities of wine-drinking France and of beer-drinking Germany, supply us with a complete scale of temperature and of atmosphere. Again, the variety of races contained in London minimizes any inference based upon mere nationality. It is clear that the liability of the Londoner is due neither to race nor to climate. Neither is it the direct result of

life in a large town, since there are large and foggy towns in which gout does not prevail.

A leading share thus clearly falls to the well-known peculiarities of the London workman's dietary. It was Sir A. Garrod's original opinion that the more liberal diet and the addiction to beer of a special kind are the most likely agents in the lead-gout of London, and the same view still commends itself to us.

The case of the German workman, likewise a liberal partaker of malt liquor, enables us still more closely to identify the precise source of the trouble. The beer of Germany is well known to be widely different from English beer. Stout is not only of higher alcoholic percentage, but is the result of a different mode of fermentation, and, especially, contains a much larger amount of nutritive material. Within the British Isles the main difference as regards beverage between the London leadworkers and those of Ireland and of the North is that with the latter the consumption of beer is not prevalent, spirits being the favourite drink.

The Share of Alcohol in the Ætiology of Lead-Gout.— Diet and beverage being jointly answerable for the lead-gout of London artisans, which of the two agencies is the most active? Here, again, conclusions may be derived from the contrast observed in plumbism.

Granted that the subjects of lead-intoxication are predisposed to gout, their indulging freely, or even to excess, in spirits certainly does not lead to the affection. This is amply proved by the observations of Christison and of others. In France, even the heavy wines from the South, largely consumed by every class of workmen, fail to cause gout among lead-workers. Lastly, in Germany lead-gout is not induced by the lighter beer so largely consumed.

If, then, as may fairly be concluded, the amount of

alcohol contained in the London workman's daily stout would not of itself produce gout, the harm must arise in connection with the non-alcoholic constituents—the solids, including the salts, but, above all, the dietetic nutritive solids, viz., sugar and partly fermented malt.

Here again the question arises whether in themselves these disguised alimentary supplies would have any effect whatever if taken in some other form in addition to the diet; or whether any special action must be attributed to the way in which their ingestion is associated with that of so much alcohol. An inquiry into the clinical history of lead-workers who happen to be teetotalers would be indicated in connection with this point. These matters, as well as the dietetic question as a whole, will be discussed more fully under the heading of diet.

Thus far, then, we have brought the problem to a partial solution: the gout of lead-workers is probably dependent upon some peculiarity of intimate nutrition, which can be traced outwardly to an obvious difference in alimentation.

## THE 'LEAD KIDNEY,' AND ITS ÆTIOLOGICAL RELATION TO GOUT.

The Excretion of Uric Acid in Plumbism.—Various observers have traced a close analogy between the renal lesions of gout and those of plumbism. Garrod has, moreover, insisted on the diminished excretion of uric acid in lead-intoxication,\* and based on these two observations a provisional explanation of lead-gout.

\* On the other hand, Gubler and Robin (quoted by Rendu, loc. cit., p. 187) find the urine of lead patients more closely analogous to that of hepatic cirrhosis—'scanty, and charged with pigments and urates'—and analogous also to those specimens among the gouty urines analyzed by Bouchard and Lecorché, in which both urea and uric acid were increased.

Uric acid is, according to Garrod, very difficult to discover in the blood save in cases of gout, but is almost invariably present in cases of lead-poisoning, independently of gout.

The excretion of uric acid was found by Garrod markedly diminished after the administration of the metal. Moreover, 'a very peculiar phenomenon was observed, namely, that after the drug had been given for a day or so, a sudden arrest of the excretion of uric acid ensued, and the function of the kidneys then became more or less intermittent; and this, it will be remembered, was also found to be the case in patients suffering from chronic gout.'

'It would appear, therefore, that in individuals impregnated with lead the blood becomes loaded with uric acid, not from its increased formation, but from its imperfect excretion; and this is of much interest in connection with the fact that the subjects of lead-poisoning are, cæteris paribus, more liable to be affected with gout, and, as we shall find further on, that those who inherit the gouty diathesis are more likely to become poisoned by the imbibition of lead.'

'Before concluding this subject, I may mention that I have seen several cases in which the medical administration of lead salts has caused severe attacks of gout in patients who had previously suffered from the disease; and the attacks have recurred so frequently whenever the medicine has been renewed, that there could be no doubt that the phenomena stood in the relation of cause and effect to each other.'\*

The Renal Changes due to Lead.—The damaging effect of lead on the kidney has been studied by Charcot and

<sup>\*</sup> Garrod, loc. cit., p. 243.

Gombault\* in guinea-pigs fed with white lead. The kidney was not affected in the acute cases; but in chronic intoxication it first suffered intratubal epithelial changes, which were followed by interstitial disease in patches, and ultimately by granular atrophy.

The same results have been obtained by Prevost and Binet, and by Ellenberger and Hofmeister (quoted by Levison, *loc. cit.*, p. 58).

#### CONCLUSIONS

In spite of this similarity, both structural and functional, between gout and plumbism, it may be contended that the proclivity to gout set up by chronic lead-intoxication is not mainly, if at all, due to the state of the kidney. Before admitting that it was so, we should require evidence that the renal lesion induced by lead in London workmen, and their resulting renal disability, were more marked than in any other subjects. Were the lesion to be regarded as a constant factor, not varying with locality, we should expect at least a proportion of gouty cases among lead-workers in every other part of the world. The practical immunity reported from most quarters is a serious difficulty in our accepting the renal inadequacy theory of Garrod.

If renal inadequacy were mainly responsible for the result, we should expect a larger incidence of gout in other types of kidney disease among those equally addicted to stout and high living. It is not in plumbism alone that kidney changes involving diminished function prevail without any gout being produced. A very large proportion, if not the majority, of the cases of chronic renal disease run through their stages without any gout being developed. This objection would be yet stronger, were it

<sup>\* &#</sup>x27;Archives de Physiologie Normale et Pathologique,' 1881.

not possible to argue that the severity of the renal disease may be in itself, owing to the cachexia and debility which it sets up, a protection against any gout—a point to be kept in mind in ætiological discussions.

The matter is not, however, quite so simple. admitted that the liability to lead intoxication is not everywhere the same in proportion to the exposure.\* It was long since pointed out by Garrod that plumbism develops earlier and in a more severe form in the gouty than in other subjects, and it is possible, as suggested by Duckworth, that in London, although new-comers are by no means exempt, the tendency to gout may be inherited by many of those who develop lead-gout. Thus, the theory of renal inadequacy does not receive much support from a study of cases of lead-gout; and the share attributable to renal defects would dwindle almost to vanishing if it were to appear that the combination most favourable to the development of gout, as well as of leadgout, was a minimum of kidney disease with a maximum of digestive efficiency.

Our inferences thus far enable us to add another important general proposition to that previously derived from a study of leucocythæmia, and of other diseases accompanied with uricacidæmia. It was shown that gout does not consist merely in an excess of uric acid. It is now clear that gout is not produced by lead per se, and that gout is not due to alcohol per se.

As regards the ætiology of lead-gout, our conclusions of a negative kind may be summed up as follows:

<sup>\*</sup> Christison's original report as to the absolute infrequency in Edinburgh of lead-intoxication, as well as of gout, has not been endorsed by all observers; and from various other quarters we have evidence of the frequency of various saturnine symptoms, with an almost complete absence of lead-gout.

- I. Lead-gout is not due to the destructive renal changes alone which are determined by lead.
- 2. Gout itself not being observed in the majority of cases of the various forms of nephritis, the derivation of saturnine gout from lead nephritis is not proved.
- 3. Lead-gout is not brought about by wine in France, nor by beer in Germany, nor by spirits in spirit-consuming districts in this country.
- 4. Lead-gout, as seen in London and in some other English towns, is most probably connected with the use of stout or porter; and it follows from the second proposition that it is not the amount of alcohol contained in that beverage which is answerable for the causation, though alcohol taken in that form may contribute some share. Most probably the nutritive elements in beer, and especially the mode in which they are supplied at recurring intervals, together with the special conditions of fermentation and of alcoholization, are the essential determining factors.

# FURTHER SUGGESTIONS ARISING IN CONNECTION WITH THE CHEMICAL AND PHYSIOLOGICAL ACTION OF LEAD.

Passing now to the question of the positive or direct agencies, we must repeat that, although in London and in other districts in England all classes of artisans are addicted to stout, lead-workers are afflicted with gout in a much higher proportion than any other set, and it seems impossible not to connect this fact with the influence of lead. We must regard lead as favouring the development of gout in an appreciable degree. In what does the influence consist?

The same dietetic and hygienic influences which generate gout might also favour saturnine intoxication.

There is, perhaps, some importance in the observation that the acetic fermentation of heavy beer may aid in sharpening the attacks of gout, whilst it may promote the introduction into the system, and the rapid circulation, of lead in a soluble form, or its reabsorption after previous deposition, both as an acetate and as a bicarbonate. The insolubility of urate of lead would likewise tell in two directions, favouring the retention both of the lead and of the uric acid.

Sir W. Roberts and Dr. Haig regard lead as favouring precipitation of uric acid in the tissues. Again, lead, by diminishing the alkalinity of the blood, as shown by Dr. Ralfe, would in a corresponding degree lessen the solubility of uric acid. When, therefore, every reservation has been made in favour of a possible antecedent gouty agency as predisposing to lead-intoxication, we may still regard the opposite relation as being in London the most common one, and we may provisionally draw from it certain inferences capable of throwing light on gout itself.

Assuming that we are right in refusing to recognise the renal lesions of plumbism as the chief cause at work, wherein would the influence reside? Attention has perhaps been too exclusively concentrated on the kidney. This is not the only organ to suffer. As a fact, lead exercises its evil influence upon various other structures, which may be enumerated irrespective of any attempt at defining their relative value: (1) The blood; (2) the circulation; (3) the nervous system; (4) the liver; (5) the alimentary canal. Are we sure that any of these forms of trouble may not have a share in setting up the liability?

In the blood, under the broad heading of anæmia, changes have been described in the shape and in the

size of the red corpuscles. Leucocytosis has also been recognised among the results of lead. Lastly, uricacidæmia has been described by some and denied by others. Even these coarse features are imperfectly known to us, but of the functions of the cellular elements of the blood our knowledge is imperfect, and concerning the pathological alterations in these functions we are absolutely in the dark. This is precisely one of the fields most likely to be exposed to the subtle influence of lead.

The high arterial tension observed in plumbism is a proof of increased peripheral resistance. The mechanism of the latter has been attributed to a loss of due proportion between the capillary bore and the diameter of the blood corpuscles; be this as it may, there is no doubt that a tonic constriction of the peripheral vessels is one of the results of lead-intoxication.

Vastly more important are the results which may possibly be traced to the effect of lead on the nervous system. Lead is a recognised cause of peripheral neuritis. That it acts on the nervous centres is demonstrated by the tremor, and other advanced toxic effects; but short of these there is room for slighter changes in the grey matter and in the nerves, sufficient to modify trophic and metabolic processes over wide areas of innervation. These possibilities cannot be considered as remote in relation to a disease in which nervous agencies are prominent, and in connection with the chemical demonstration of the presence of lead in the nervous centres. Nevertheless, they are for the present purely speculative.

The advocates of the nervous origin of gout and of lead-gout would find here, as in every other presentation of gout, ample illustrations for their contention. Two facts have been regarded as specially suggestive of an influence of the central nervous system: (I) The not

infrequent combination of paralyzing neuritis with arthritic or œdematous changes. (2) The observation that, in some non-gouty districts, marked arthritic changes occur, to which were applied the names 'saturnine arthropathy'\* and 'saturnine arthralgia' (a painful affection of the legs and joints occurring with the onset of paralysis, without swelling of the joints). On these points, and on the whole subject of lead-intoxication in gout, Sir Dyce Duckworth's treatise would be consulted with profit.

We are able to refer with much greater assurance to the connection with lead of well-known clinical affections of the digestive organs, the liver and intestine. Lead perhaps shows a greater tendency than other metals to be distributed throughout the body rather than collected in any one organ. This gives it additional facilities for being periodically redissolved in certain states of the blood, and circulated to the detriment of the system at large, and in particular of the neuro-muscular structures.

The most common and the most familiar of all symptoms of plumbism is its astringent effect upon the muscular fibre of the intestine; constipation is set up, occasionally leading to colic. It is unnecessary to insist on the direct influence which constipation must exercise upon digestion and assimilation. Its indirect influences are probably hardly second in importance; torpidity and congestion of the liver are necessary results of intestinal torpor, and, for all who admit that gout is essentially a disease of faulty nutrition, this represents a factor of paramount importance, with special bearing on the question of treatment.

<sup>\* &</sup>quot;Dropped wrist" is apt to present a painless tumour, with displacement backwards of the bones and distension of the synovial sheath.

#### VI.

## THE CLINICAL STUDY OF GOUT.

#### CHAPTER XXI.

#### THE CLINICAL TYPES AND STAGES OF GOUT.

THE older classification of gout into acute and chronic, sthenic and atonic, arthritic and visceral, or regular and irregular, is not open to much criticism. For working purposes something less rigid and more life-like might be welcome and of use: a classification of the patients in respect of their variety of gout, rather than of the gout apart from them. This indication is probably greater in connection with this than with any other affection, if we regard it as a deviation of the normal functions, rather than as a morbid entity capable of being considered apart from its bearer. Indeed, its clinical and pathological study cannot be profitably attempted without some preliminary acquaintance with its multiple forms.

Let alone the great variety of constitutions upon which gout may be grafted\*—a complex study which must be

<sup>\*</sup> Duckworth (*loc. cit.*, p. 455) draws attention to Laycock's teaching, that the varieties of gout depend on the varieties in the constitutions. All diatheses are liable to gouty affections, but each of them modifies the gouty symptoms and evolution. He recognised the following varieties: (1) The sanguine arthritic or 'John Bull' type, with prevalence of sthenic and regular paroxysms; (2) less common, the

deferred—there are broad clinical types presenting contrasts of the first order.

To the elementary distinction between acquired and inherited gout we need not refer, beyond repeating that all hereditary gout, if traced sufficiently far back, is originally acquired gout.

Groups I. and II.—Two well-defined types occur at the top and at the bottom of the long list of degrees and varieties. At one extremity is gout limited to a single acute attack, preceded and followed by a condition of practically perfect health; at the other gouty cachexia, the result of many years of constantly recurring gouty troubles.

Groups III. and IV.—The intermediate types need not be defined in full detail. The mitigation of the worst type forms the class of inveterate gout with moderate cachexia; and we are familiar with a large class of cases related to Group I. in which acute attacks recurring at long intervals are separated by periods of sound or robust health.

Group V.—A very large and heterogeneous group is made up of all those cases, too varied to repay further classification, the common features of which are: (a) the mildness of the arthritic troubles, and (b) the prominence of the constitutional element of gout, with a tendency to visceral, nervous, and cutaneous complications. This group comprises most of the cases of inherited gout and of gout in the female. It corresponds in great part to the

bilious arthritic type, apt to be asthenic, and to develop earlier; (3) the 'nervous arthritic' type. Two forms of gouty disposition were included in this category, one being complicated with struma, viz., the 'neuro-arthritic type proper,' with tendency to affections of the cerebro-spinal axis, with its nerves and membranes; the other with the sanguine or the bilious type, viz., the 'neuro-vascular or vaso-motor' type, in which the circulation of the nerve-centres suffers by reason of altered vaso-motor action' etc.

group sometimes termed *irregular gout*. Most instances of *atonic gout* also belong to this category. Lastly, it includes also the attenuated forms for which the term *goutiness* has been proposed.

Group VI.—Lead-gout is sufficiently differentiated by some of its peculiarities to be described independently of other forms. Some of its characteristics assimilate it closely to Group V.

Sub-Varieties.—In each of the groups special peculiarities give occasion for further sub-division. Thus in chalky or tophaceous gout, the local deposits of biurate or tophi, which may occur in any of the groups, are specially abundant. This feature is of marked frequency in the group of cachectic cases.

Another important clinical sub-variety is that in which gout develops in the subjects of constitutional *lithiasis* or gravel. Many of these are cases of inherited gout, and most of them belong to Group V.

The albuminuric variety is not restricted to any of the types, but it is most common in inveterate gout and in gouty cachexia; the latter is largely brought about by the evil influence of kidney disease.

Most of the diabetic and glycosuric cases belong to Group V., but the affection may also occur in the other groups.

Gouty metastasis, sometimes termed *metastatic gout*, does not constitute a nosological group: it is merely an accident of which each of the groups mentioned might furnish instances.

Again, visceral gout is a convenient general heading for the numerous abarticular manifestations to which all gouty subjects are liable, but the chief contingent of cases is furnished by Group V.

Suppressed or retrocedent gout is the most striking and

ominous mode of visceral gout, and much clinical and literary attention has been devoted to it.

No practical object would be served by extending our list of sub-varieties, but a systematic clinical study will imply separate consideration of the clinical aspects of gout in connection with the chief organs and functions. The description of the symptoms of gout will be given under corresponding headings.

## THE CLINICAL ANTECEDENTS OF ACUTE GOUT: THE PRE-ARTHRITIC STAGE.

A first fit of the gout, coming unawares upon a man of healthy parentage and antecedents, prompts us to inquire, What was the previous state shortly before the fit? Was he perfectly sound previous to the two or three days of premonitory indisposition? or was he gouty? The question has practical as well as pathological importance.

We have been in the habit of looking upon the fit of gout as a climax, the result of long persistence in habits conducive to the disease. Do the facts always bear out this view? The chief difficulty occurs in the cases included under the clinical Group I., in which the patient has one fit and never another, and might in later years almost pass for a non-gouty subject, but for his own report of a bad attack of gout in the toe many years previously.

On the other hand, a patient who has never consciously suffered from articular troubles is not infrequently pronounced by competent observers to be 'gouty.' The recognition of a pre-arthritic constitutional change would enable us to connect with gout cases of this sort who, according to the more strict definition of the disease as an essentially arthritic affection, could not be included.

Many a patient who has never had, and perhaps never may have, articular gout presents symptoms usually observed in those who are confirmed gouty arthritics; and it is during this pre-arthritic stage, whether acquired or hereditary, that the various manifestations sometimes spoken of as *irregular gout* are apt to arise, and to be rightly or wrongly ascribed to the gouty influence.

Sydenham describes the onset of the fit as sudden. Yet the fact that in a few cases a slow preliminary implication of the joints may precede the acute attack for some length of time suggests a provisional distinction between (I) a 'pre-arthritic' stage in the full sense of the term, and (2) a silent or 'quiet arthritic' stage—the gouty attack being sometimes preceded by the first only, in other subjects by the second also.

Latent Arthritic Gout.—Autopsies being unusual in this disease, it is difficult to form a correct estimate of the proportion of cases in which the arthritic form may have been *latent* in those who had presented for clinical observation only the so-called irregular symptoms of gout.

Uratic incrustations have sometimes been reported in the joints of those who, so far as could be ascertained, had never suffered from any arthritic symptoms. These are instances of an absolutely *latent* deposition of uric acid. In the absence of a *post-mortem* examination, if put down to gout at all, they might have been clinically reckoned as pure instances of *pre-arthritic gout*, and classified as entirely free from all joint implication. This possible fallacy must be carefully borne in mind in every discussion of the dictum, 'Without uric acid in the joints, no gout.'

Quiet Arthritic Gout.—Cases of quiet gout form a distinct and large group. Here the joints are obviously implicated; digital nodules, or even small tophi, are present, and there is some impairment in movement. The arthritic changes, however, are altogether chronic, and almost painless, and in that state they may continue for considerable periods of time. Indeed, here again an acute arthritic attack may never make its appearance. This form is specially common among women, and is capable of being mistaken for osteo-arthritis. Again, tophaceous gout may proceed to considerable developments before it is complicated with any genuine acute attack, although the formation of tophi is very apt to follow the acute seizures. Tophi in the auricle are of every-day occurrence where no definite warnings of gout have been experienced.

Greater uniformity would be established between the various clinical types were it obvious that the gouty seizure is never a primary event, and that in all cases a pre-arthritic gouty stage occurs. In many cases gout undoubtedly precedes the acute joint troubles, and in some these never come about, in spite of a long continuance of goutiness.

Diametrically opposed to these instances of gout, whether hereditary or acquired, in which the constitutional change is manifest, but the articular implications are almost indefinitely delayed, or apt to be of the asthenic and chronic type, is the large class of acquired, sthenic gout in which the pre-arthritic stage is latent or of vanishing duration. In them, if present at all, this period is one of silent and slowly progressive general nutritive changes, the treatment of which is usually neglected. The nature of these pre-arthritic changes is matter of pure speculation; we only know that they result in a structural delicacy akin to degeneration, which is transmissible by inheritance, and the long continuance of which in the individual tends towards the so-called gouty cachexia. This final stage, however, is never reached except through a long period of joint-trouble; and opinions are still

divided as to whether the constitutional or the local trouble should be blamed for the mischief.

How long the pre-arthritic or evolutionary stage may continue, or whether, once originated, it may ever be arrested, we have hitherto no means of judging. In slight cases, under the influence of appropriate treatment or diet, it is conceivable that the advent of the arthritic period might be indefinitely delayed. Under this inhibitory treatment the patient's condition would be analogous to that of persons inheriting a strong tendency to gout, but who may, nevertheless, permanently escape any arthritic implication.

In conclusion, the duration of the pre-arthritic stage must remain an open question, so long as we are in ignorance as to the nature of the changes themselves, and as to the elements of variability special to individual temperaments and circumstances. The more stormy attacks in the robust often seem to have been preceded by the least premonitions. These are also the cases which sometimes seem to throw off the gout for long periods, as though the impression made on the nutrition of the tissues had been a transient one only, and any changes in the latter purely superficial. In others, however, the acute attacks pass away, but the constitutional state remains.

There would appear to be more real danger to health in the evolutionary stage than in the acute attack. Indeed, the acute attack has long been regarded in a sense as curative and as a clearance for the system. According to Sir A. Garrod, the deposit may be partly destroyed by the attack, and Sydenham held that the *materia peccans* might be got rid of by insensible perspiration or otherwise.

#### CHAPTER XXII.

#### THE ACUTE ARTHRITIC ATTACK.

Sydenham's description of the acute attack has never been surpassed, and will never cease to be quoted.\* It will be found to agree with those given by the most recent

\* 'Towards the end of January or the beginning of February, suddenly and with scarcely any premonitory feelings, the disease breaks out. Its only forerunner is indigestion and crudity of the stomach, which troubles the patient for some weeks previous to the attack. His body also feels swollen, heavy, and windy, symptoms which increase from day to day until the fit breaks out. A few days before this, torpor comes on, and a feeling of flatus along the legs and thighs. Besides this, there is a spasmodic affection, whilst the day before the fit the appetite is unnaturally hearty. The victim goes to bed in good health and sleeps. About two o'clock in the morning he is awakened by severe pain, generally in the great toe; more rarely in the heel, ankle, or instep. This pain is like that of a dislocation of the bones of these parts, and is accompanied by a sensation as of chilly water poured over the veins of the suffering joint. Then follow chills and shivers, and a little fever. The pain, which was at first moderate, becomes gradually more intense, and while it increases, the chills and shivers die out. Every hour that passes finds it greater, until at length at night-time it reaches its worst intensity, and insinuates itself with most exquisite cruelty among the numerous small bones of the tarsus and metatarsus, in the ligaments of which it is lurking. Now it is a violent stretching and tearing of the ligaments, now it is a gnawing pain, and now a pressure and tightening. So exquisite and lively meanwhile is the feeling of the part affected, that it cannot bear the weight of the bedclothes nor the jar of a person walking in the room. Hence the day is passed in torture, and a restless rolling, first to one side then to the other, of the suffering limb, with perpetual change in posture; the tossing of the body being about as incessant as the pain of the tortured joint, and being at its worst as the fit is

authorities, and in particular by Sir A. Garrod, according to whom the events are about as follows:

Good health—sometimes unusually good health—may immediately precede the acute sthenic attack. At 1.0 to 4.0 a.m. the patient wakes, frequently with slight shivering, and with more or less pain in the ball of the toe. Feverishness follows, whilst the pain increases. It is described as 'burning, throbbing, with tension and stiffness.' After some hours partial relief is obtained and ushered in by gentle perspiration. On waking in the morning, the patient finds the toe swollen, the skin tense and shiny and exquisitely tender, with distended veins.

coming on. Hence the vain efforts by change of posture, both in the body and the limb affected, to obtain an abatement of the pain. This goes on towards the second or third hour of the morning (a whole day and night after the first outbreak of the fit), such time being necessary for the moderate digestion and dispersion of the peccant matter. The patient then has a sudden respite, which he falsely attributes to the last change of position. A gentle perspiration is succeeded by sleep.

'He wakes freer from pain, and finds the part recently affected swollen. Up to this time the only visible swelling had been that of the veins of the affected joint. Next day (perhaps for the next two or three days), if the generation of the gouty matter have been abundant, the part affected is painful, getting worse towards evening, and better towards morning. A few days after, the other foot swells, and suffers the same pain. The pain in the latter regulates the state of the one first attacked, for the more acutely it is tortured, the more perfect is the abatement of suffering and the return of strength in the other. Nevertheless, there is a repetition in the second case of all the misery of the first, both as regards intensity and duration. Sometimes during the first days of the disease the peccant matter is so exuberant that one foot is insufficient for its discharge. It then attacks both, and that with equal violence. Generally, however, it takes the feet in succession' ('A Treatise on Gout and Dropsy.') (The works of Thomas Sydenham, M.D., translated from the Latin edition of Dr. Greenhill, with a life of the author, by R. G. Latham, M.D., etc., in two volumes. London: printed for the Sydenham Society, MDCCCL. Vol. ii., p. 121 et seg.).

In the worst cases the pain is intolerable, the slightest vibration or the slightest weight calling forth fresh agony. During the day it may still be severe, but its return is generally delayed until the second night. This alternation may proceed for days, or in a modified form for weeks.

First attacks, and often subsequent attacks, usually implicate the ball of one great toe only, sometimes changing over to the other great toe or sometimes travelling to the inner side of the foot.

'When the attack, or, more properly speaking, the series of attacks, is about to terminate,' the local tension, swelling, redness and vascular fulness lessen, the skin pits on pressure, and itching of the skin, with desquamation, soon follows.

In the minor attacks, to which Garrod refers as the 'acute asthenic gout,' feverishness may be absent, there is less swelling, heat, and redness; but œdema, with subsequent itching and peeling, are observed. Garrod observes that this lesser form is more apt to lead to permanent mischief than the worse gouty seizures.

Anorexia, thirst, constipation, a high-coloured, scanty urine, turbid on cooling, are part of the usual type. Severe cramps in the legs may aggravate the discomfort.

Premonitions, usually absent prior to the first attack, are almost the rule in later ones in the shape of disturbance of digestion, 'heart-burn, acidity, flatulence, drowsiness after food, hiccough, confined bowels, loss of appetite, lowness of spirits, and a feeling of lassitude.' The individual weakness or symptom is apt to assert itself, and usually there is much irritability of nerves or temper. The premonitory symptoms, and, in particular, the frequent bronchitis, are relieved on the advent of the fit 'The urine before an attack is usually scanty and highly

coloured, but sometimes, on the other hand, very copious and pale.'

In spite of the appearances so suggestive of the formation of pus, gouty inflammation is not followed by suppuration. Garrod doubts whether a *first fit* of the gout has ever been recorded in which suppuration took place.

Among the general symptoms, all of which are regarded as induced by the local condition, and are not, as often in rheumatic fever, out of proportion to the articular trouble, the feverishness, acceleration of pulse, thirst, anorexia, all vary with the severity of the local inflammation.

The temperature of the axilla 'ranges from 99° Fahr. to 104° Fahr., most commonly from 100 to 102 where many joints are involved, and from 99 to 100 where one or two only.

Although 'intense heat of the joints' is complained of, the surface thermometer does not record a marked rise.

The skin, at first dry, becomes moist without ever presenting the heavy sweats of acute rheumatism.

The tongue is furred; anorexia, thirst, and often constipation, with obvious portal congestion, occur. As a whole the digestive system is much upset, though in a few cases it escapes. The enlargement of the liver may be purely temporary, or may have existed as one of the ætiological factors of gout.

The pain is characteristic. By those who are in a position to compare, it is felt to be different from other pains, whether rheumatic or from injury. 'It often precedes the other signs of inflammation, is more localized, and generally at first confined to a spot on the side of the joint; whereas in acute rheumatism the pain extends throughout the whole articulation.' Sir A. Garrod has

met with cases, now so common, of a first attack of gout in which the severity of the pain was not in proportion to the apparent signs of inflammation.

The following is Sydenham's description of the pain:

'When the disease is confirmed, the ligaments of the ankle-bones feel as if wrenched or squeezed by a strong hand when the patient stretches himself of a morning. At times, without any stretching at all, there is this pain, and just as the patient is going to sleep he feels as if the ankle-bones were suddenly crushed by a heavy blow, and he wakes with a cry. The tendons of the muscles of the ankle are seized with a pain so intense that if it were permanent it would wear out human patience. . . .

'Sometimes the thigh feels as if a weight were attached to it, without, however, any intolerable pain. It descends, however, to the knee, and then the pain is intense. It checks all motion, nails the patient down to his bed, and will hardly allow him to change his posture a hair's breadth. . . . The least contrary movement causes pain, which is tolerable only in proportion as it is momentary. This movement is one of the great troubles in gout, since with perfect quiet the agony is just tolerable. . . . One thing, however, is constant: the pain increases at night and remits in the morning.'

'The mind suffers with the body, and which suffers most it is hard to say. So much do the mind and the reason lose energy as energy is lost by the body, so susceptible and vacillating is the temper, such trouble is the patient to others as well as to himself, that a fit of gout is a fit of bad temper. To fear, to anxiety, and to other passions, a gouty patient is the continual victim, while, as the disease departs, the mind regains tranquillity.'

The ædema is also characteristic, and a valuable guide in the diagnosis from rheumatism, in which it is quite

exceptional, although the pitting cannot be readily obtained until the acute tension is lessened.

The desquamation, which is often preceded by much itching, occurs after the acute symptoms have subsided, and is thought by Garrod to be induced by the previous œdema.

As suggesting a derivation of the ædema from the toxic influence of some blood impurity, Garrod notices the local ædema also observed in gonorrhæal rheumatism and in pyæmia.

This is Sydenham's description of some of the symptoms which have been enumerated:

'For the first fourteen days the urine is high-coloured, has a red sediment, and is loaded with gravel. Its amount is less than a third of what the patient drinks. During the same period the bowels are confined. Want of appetite, general chills towards evening, heaviness, and a trouble-some feeling at the parts affected, attend the fit throughout. As the fit goes off, the foot itches intolerably, most between the toes; the cuticle scales off, and the feet desquamate as if venomed. The disease being disposed of, the vigour and appetite of the patient return, and this in proportion to the violence of the last fits. In the same proportion the next fit either comes on or keeps off. Where one attack has been sharp, the next will take place that time next year, not earlier.'

A diagnosis between acute gout and acute rheumatism is not always easy. In the past mistakes have undoubtedly occurred. It is important to remember this circumstance in connection with some of the older records of metastasis of gout to the viscera, and particularly to the heart.

In Garrod's experience the formation of chalk-stones on a large scale may, but this is the exception, follow soon after the acute attack. 'Permanent stiffness or complete ankylosis may result from a first attack, even though unaccompanied with much local inflammation or enlargement.'

The Duration of the Attack.—According to Sydenham, 'In strong constitutions, where the previous attacks have been few, a fortnight is the length of an attack. With age and impaired habits, gout may last two months. With very advanced age, and in constitutions very much broken down by previous gout, the disease will hang on till the summer is far advanced.'

'Now, a series of lesser fits like these constitute a true attack of gout, long or short, according to the age of the patient. To suppose that an attack two or three months in length is all one fit is erroneous. It is rather a series of minor fits. Of these the latter is milder than the former, so that the peccant matter is discharged by degrees, and recovery follows.'

#### THE CHARACTER OF THE ACUTE LOCAL LESIONS.

The aspect of the local inflammation is that of a phlegmon; but though vascular changes occur, they are not due, so far as we know, to any infective inflammatory process. Rarely do we hear of any suppuration in or around an acutely gouty joint. On the other hand, the vascular reactions are singularly prominent, and as sudden, as rapid, and as severe, as in any common inflammation accompanied with diapedesis. The non-occurrence of phlegmonous diapedesis is also a feature of rheumatic arthritis, which differs from the gouty both in its aspect, in the obvious degree of the lymphatic disablement, and in the absence of subsequent desquamation, an almost invariable sequel in gout.\*

<sup>\*</sup> Scudamore states that, of 234 cases, 78 had never presented this sign.

To what extent and in what manner the arthritic attack may influence the constitutional state of the patient is a question upon which clinical evidence is conflicting. Sydenham regarded the attack as the means of clearing the system of the *materia peccans*, and Garrod regards the local inflammation as able to destroy part of the local accumulation of biurate. In other cases the opposite result is observed.

At any rate, no fixed proportion seems to exist between the severity of the arthritic seizure and the constitutional consequences. These in some fortunate instances will not appear after a single sharp attack or a series of attacks, whilst profound changes are observed in many whose attacks have never been so severe, though more frequent.

#### THE JOINTS AFFECTED.

The great toe is the first to suffer in a great majority of cases. A satisfactory explanation of this striking liability has never been given. It has been suggested that, of all joints, it is worked hardest, or, at any rate, most constantly; yet, as in hard-working labourers it is not the subject of gout, it might even be argued that in most patients it has not been worked hard enough.

Moreover, after all said, each joint in our body is made for the express purpose of being used, but this, one of the most active of our nether joints, is rarely allowed the full freedom which it claims. None of our joints is so much hampered as that of the toe by shoe-leather. Even the sandal of the ancients must have interfered with its full flexion. Its exercise is taken under adverse, and too often painful, restrictions as regards room and proper circulation. Few make a point of giving it at times a hygienic holiday. Sir A. Garrod mentions its abundant fibro-vascular tissues, its remoteness from the heart, its exposed position, rendering it obnoxious either to direct violence or to the danger of false steps—and to various injuries of which he has traced the results in the bodies of those who had never had the gout.

We are reminded also of the peripheral position and the heavier column of blood, which favour local congestions. All these influences had been noticed as possible determining agencies by Boerhaave and Van Swieten.

The great toe may be the first joint affected because of its more universal and constant use even by those whose hands are relatively inactive, and because the wrenches and strains which predispose to the gouty deposit are more likely to occur when the joint does not work true, its axis having been thrown out by the continued pressure of ill-fitting boots.

None of the alleged reasons are really satisfactory, and the question remains one for speculation. Thus, Sir A. Garrod reminds us of the attraction of certain poisons for definite parts of the body, and questions whether this influence may not have something to do with the early selection of the great toe by the gouty affection.

The order in which the various joints are successively affected is, according to Garrod (loc. cit., p. 291), about the following: (1) The great toes; (2) the heels; (3) the ankles; (4) the knees; (5) the small hand-joints; (6) the elbows; and lastly, the shoulders and hips.

Garrod\* found that in no more than 5 per cent. were other joints implicated, to the exclusion of the great toe; and he quotes Dr. Braun's forty cases, thirty-six of which occurred in the toe, two in the heel, one in the knee, and one in the hip also.

<sup>\*</sup> Loc. cit., p. 18.

Sir Charles Scudamore\* gives a table of 516 cases, in which the part *first* affected was noted. One or both great toes alone suffered in 341, or nearly two-thirds; in 373 the great toe was attacked, together with some other part. In less than twenty cases out of the whole was the lower extremity not included among the parts affected.†

Among the localizing factors, besides the predisposing occurrence of previous mechanical damage, Garrod lays great stress on *cold*. The hip-joint, which is rarely affected, is by its proximity to the trunk kept at an evenly warm temperature; that of the knee, which suffers much, is frequently depressed, and that of the foot yet more often.

He notices that in the case of more superficial deposits the spots selected are also those of a relatively sluggish circulation. The ear is specified as an instance of both peculiarities.

The extension of the process from the single joint originally attacked to many joints may be regarded in the light of an overflow of the accumulating store of urates from the parts which first attracted it to others still unencumbered.

Chemical reaction is probably an important localizing agent. In explanation of the special liability of particular tissues, 'the ligaments, cartilages, and others closely allied,' Garrod suggests that, in addition to their possessing but little vascularity, they probably are less alkaline than many other tissues, and certainly less alkaline than the blood itself.

<sup>\*</sup> Quoted by Garrod, loc. cit., p. 17.

<sup>†</sup> The following observation of Scudamore has a practical bearing: 'I find that in examples of hereditary gout the great toe has been the situation first chosen, and that the most remarkable exceptions have been in those persons who have wholly acquired the disease.'

#### CHAPTER XXIII.

# THE PROGRESS OF GOUT.—CHRONIC GOUT AND GOUTY CACHEXIA.

The original gouty attack may never be followed by another. The mode of treatment and the mode of life influence the result. A strong predisposition will, however, expose some individuals to constant recurrences on the slightest provocation. Sydenham had these in mind when he wrote: 'Up to a certain time the gout comes on towards the end of winter, lasts for two or three months, and retires regularly. Afterwards, however, it lasts throughout the whole year, except only the hottest months of the summer. Furthermore, the longer the attack in general, the longer is each individual fit. Instead of a day or two, they last a fortnight. Instead of the feet, they attack any joint indifferently. Lastly, on the first or second day after, the patient, besides the pain, has loss of appetite and general discomfort.'

'Until the disease has reached a certain degree of severity, the patient enjoys long intervals between the fits, and during these intervals good health. . . . After it has attacked each foot, the fits become irregular, both as to the time of their accession and duration.'

The accuracy of this description has been confirmed by all observers. Garrod states that the autumnal fit is not usually added until several of the annual attacks have recurred in spring. He mentions, however, exceptional cases 'who suffer more in summer than at any other time of the year.'

Thus, the individual clinical history of gout will take very different forms. It may be limited to one or two acute attacks in the great toe, the gout never passing into the chronic stage. Or it may consist of a series of seizures occurring at first at distant intervals and timed by the seasons, but gradually becoming more and more frequent and irregular in their appearance. Still, as pointed out by Garrod, this frequency may not be associated with any wide distribution of the joint affection, nor with extensive damage to the joint structures; and the liability may last only for a period of years, and ultimately cease before old age.\*

A totally different picture is afforded by the more severe types of chronic gout, the deforming and crippling arthritic varieties, and gouty cachexia. It is not uncommon for these forms of affliction to be combined in the same subject; indeed, the question has never been settled as to whether the cachexia arises from the joint disease, or whether the joints suffer most because of the constitutional decay. At any rate, an inevitable downward progression is obvious in both sets of cases.

The Crippling Form of Chronic Gout.—It suffices for an early acute attack to have, as rarely happens, set up

<sup>\*</sup> The mitigation of the arthritic symptoms of gout with the decline of life has long been known. Sydenham refers to it in the following words: 'After many torments, when death is about to relieve the patient, the fits become milder. . . . Then, instead of the usual pain, there is uneasiness, pain in the stomach, weariness, and sometimes a tendency to diarrhæa. These symptoms ease the pain. The pain abates these symptoms. . . . When gout has gone on for many years, the fits grow easier, and the patient is worn out by weakness rather than by pain.'

ankylosis in one of the joints of the lower limb to henceforth introduce into the patient's clinical history a new
factor—that of restricted movement, or even of relative
immobility. This is in all cases a serious aggravation of
any previous predisposition to the disease, distinctly
favouring its further developments. It is the more remarkable that many thus afflicted do not go from bad to
worse, but maintain a comparative level of general health
and relative freedom from local manifestations. With
others, probably of less robust health originally, or less
careful of the rules of hygiene, the results are painful to
witness; more and more joints become implicated and
useless, until the patient's life is a burden.

Sydenham gives a graphic account of the crippling effects of gout: 'Sometimes it distorts the fingers; then they look like a bunch of parsnips, and become stiffened and immovable. This is from the deposit of chalk-stones about the ligaments of the knuckles. The effect of this is to destroy the skin and cuticle. Then you have chalk-stones like crabs' eyes exposed to view, and you may turn them out with a needle. Sometimes the morbific matter fixes on the elbows, and raises a whitish tumour almost as large as an egg, which gradually grows red and inflamed.

'Eventually the limbs become drawn up and contracted.
... The more, too, the patient strives to walk, under the idea of strengthening his feet, and thereby rendering them less liable to the disease, the more likely is the peccant matter, which has never yet been fully discharged, to be thrown upon the inward parts. Herein is the great danger.'

Progressive failure of health is largely explained in the case of the crippled person by the discomfort, the pain, and the mental disappointment, and, above all, by the loss of that minimum of exercise which is the preventive

of gout, and may even sometimes be regarded as its cure.

Sir A. Garrod's cases of chronic gout presented a considerable amount of uric acid in the blood.

The *urine* of chronic gout is described by Garrod as being 'rather paler than healthy urine, of lower density, and increased in quantity. The amount of urea, except in extreme cases, remains much as in health, the character of the diet being taken into consideration. The uric acid is very much diminished, and liable to be excreted in an intermittent manner. A small amount of albumen is very frequently present. The occurrence of deposits in the urine is not common; they occasionally fall during the cooling of the fluid, either in the form of urate of soda or as rhombs of uric acid, more or less coloured.'

# THE VARIETIES OF CHRONIC GOUT.

Sir Dyce Duckworth,\* in his masterly analysis of this subject, describes, in addition to gouty cachexia, two main varieties of chronic gout—the 'tophaceous' and the 'deforming.'

Tophaceous Gout, or Chalky Gout, is characterized by uratic deposits, often of great size, in the neighbourhood of the joints, distending the skin, which may give way and exude a creamy fluid. This secondary softening of the deposit is usually not due to suppuration, though in broken-down constitutions abscess may form, the discharge then consisting of pus in addition to the sodium and calcium urate, to calcium phosphate and sodium chloride, which are the usual constituents. The outflow of urates may be considerable; whilst it lasts, and for some time afterwards, the patient seems to be protected against fresh articular attacks.

<sup>\*</sup> Loc. cit., p. 254 et seq ..

The tophi may be in direct communication with the joint, or, as in the case of the subcutaneous infiltrations and of bursal tophi, situated at a distance from it.

The skin in the vicinity of the tophi is thin, glossy, and often purplish from venous congestion.

Tophi, according to Duckworth, and especially those in the ear, may precede, even by some years, the arthritic attacks; or, on the other hand, they may, even without the occurrence of ulceration, partly disappear under the influence of repeated arthritic attacks, fresh tophi being developed.

Tophaceous gout is more common in the male sex. It is usually associated, sooner or later, with gouty renal disease.

Chronic Deforming Gout is largely made up, according to Duckworth, of arthritic changes analogous to those of osteo-arthritis, with a minimum of uratic infiltration. Deformity, deflection, dislocation, ankylosis, true or false, are associated with overgrowth of cartilage and of bone, erosion, uratic incrustation, moderate synovial effusion, and crackling on movement, though none of the characteristic changes are so extreme as in osteo-arthritis. The extent and rapidity of the local changes does not bear any constant relation to the severity or frequency of the paroxysmal attacks. Individual peculiarity largely influences the articular degenerations. Implication of bursæ is common, and cutaneous uratic infiltrations may occur. The crippling effect is great, especially when the knee or ankle is affected.

Duckworth associates with the description of this form that of the chronic painful affections of tendons and fasciæ, particularly those of the foot (heel and tendo Achillis, plantar fascia, tarsus, etc.) and the extreme deflections of digits and toes. Analogous chronic changes, again, are those limited to the knotty enlargement of the small joints, and to the formation of Heberden's nodules, and usually (especially in women, who are more subject to them) connected with a history of visceral and nervous rather than of articular symptoms, and in that sense not strictly to be included under the heading of chronic gout. Duckworth suggests incomplete gout as their proper category.

In the entire group, although organic and particularly renal complications are apt to occur, there is less tendency than in the tophaceous group to cachexia and to early break-down. Life may long be spared, in spite of some renal, cardio-vascular, and pulmonary (emphysematous) change.

#### GOUTY CACHEXIA.

Gouty cachexia is the extreme expression of that faulty metabolism which is at the root of gout, and we may note that it is not restricted to, though perhaps more common in, those whose uratic deposits have been most abundant. It is a late development, except under the accelerating influence of strong hereditary predisposition or of depression, which may determine its advent in early middle age. Duckworth has once exceptionally seen it in a woman at forty. He traces the occurrence of cachexia either to original frailty of constitution or to that which is induced by unbridled indulgence in the predisposed. Truly robust constitutions do not suffer in this way, or only late, though they may have the gout often and severely. Persistent energy of digestion and plentiful supplies, though they may feed the gout, doubtless ward off the cachexia.

In the light of modern pathology we trace many of the varied symptoms of the condition in question to the organic changes which form its substratum. Ultimately all the tissues suffer, as a result partly of the original gouty malnutrition, but very largely of the secondary organic disease.

In gouty cachexia we are obviously dealing with the results of deep-seated changes, which no longer admit of correction, and with deviations of nutrition based upon the organic defects,\* and henceforth incapable of being rectified. The chief organic failures are those connected with the blood, with the organs of digestion, and particularly with the stomach and liver, and with the kidney.

Pallor is a striking feature of the average gouty cachectic person. It is probable changes in the blood ultimately take place, though, as elsewhere pointed out, anæmia is not a characteristic of early gout.

The failure of digestion is greatly due to the circumstances just mentioned. At an earlier date it is in obvious connection with hepatic derangements † and nervous disturbances. We need not dwell here upon this aspect of gouty cachexia.

The organic changes occurring in the kidney have already been discussed, and a great part of the cachexia of gout must be attributed to the general results of renal atrophy, casting upon the system a variety of toxic substances in addition to an unexcreted balance of uric acid.

- \* 'The peccant matter lodges in the viscera, involves their structure, impairs the organs of secretion, leaves the blood stagnant, thick, and feculent, prevents the discharge of the gouty matter on the extremities, makes life worse than death, and finally brings in death as a relief.'—Sydenham, loc. cit.
- † 'Other symptoms arise, piles amongst others. Also indigestion, with rancid tastes in the mouth whenever anything indigestible has been swallowed. The appetite fails, so does the whole system. The patient has no enjoyment of life. . . . The back and other parts itch, most at bed-time.'—Sydenham.

The general effects of renal toxæmia are greatly intensified in the specially debilitated subjects of chronic gout, and the toxic tissue-decay proceeds rapidly, with a minimum of reactionary growth. In this way may be explained the anæmia, the early fatty degeneration of the cardio-vascular system, with all the consequences implied, the atony of mucous membranes, the failure of the glandular system, and the ultimate giving way of the nervous functions, the cerebral symptoms ranging from simple depression with irritability, to amnesia, delusions, stupor, or coma. Death may occur from the usual results of combined renal and cardiac disease, or from the rupture of a cerebral vessel, or from some intercurrent acute inflammation.

Tubercular phthisis, in a small proportion of cases, is a final complication of advanced cachexia. At this stage gout does not appear to exert, as in the earlier periods, a prophylactic influence against bacillary disease. On the contrary, the lesions of phthisis are apt to run a more than usually rapid course in the unhealthy tissues of the gouty cachectic.

# CHAPTER XXIV.

# THE CLINICAL FEATURES OF GOUT AND GOUTINESS IN CONNECTION WITH THE VARIOUS ORGANS.—AFFECTIONS OF THE MUCOUS MEMBRANE.

ANATOMICAL evidence that uratic gout can affect internal organs is almost absolutely wanting. Much so-called 'visceral gout' should strictly be termed 'visceral disease in the gouty.' Clinical evidence on the contrary points to a decided influence, peculiar to the gouty state, which determines the onset, and modifies the course of visceral affections. The association with articular gout is often so close that 'visceral gout' has been allowed currency as a clinical expression, applicable to a limited number of disorders; but even in these the reservation mentioned should never be forgotten.

Without attempting an elaborate study of so wide a subject, we may profitably review the more important structures and organs in respect of their liability to gouty manifestations, reserving for subsequent consideration the abarticular symptoms of retrocedent gout.

# THE CRITERIA FOR THE GOUTY NATURE OF SYMPTOMS.

In view of this, pathologically speaking, insecure position, and of the scepticism to which an ill-judged use of the term 'gout' too often gives rise, it is desirable to define as closely as possible the conditions under which its employment is called for.

The differences between so-called gouty and ordinary inflammations occurring in the same situations may be such as would appeal only to the expert. To the general physician, from whose standpoint these pages are written, their gouty nature is usually rendered sufficiently obvious by the constitutional context, and to the specialist their peculiarities are sufficiently striking to lead to a suspicion of their constitutional cause; and in either case their proper treatment is the treatment of the gout upon which they depend.

The gouty joint bears its own diagnosis written large, but no distinctive feature attaches to the abarticular troubles, all of which may own various other causes. There is an inherent difficulty in the attempt to prove as gouty any abarticular symptoms, and especially the visceral. Many of the latter are in themselves subjective, mysterious, and without tangible lesion. The few in which definite structural changes are perceptible, as, e.g., the effusion into a tunica vaginalis, or the râles and rhonchi of a congestive bronchial attack, or the visible changes in the skin of an eczema, are therefore specially valuable as definite objects for study. Still, everywhere our evidence is clinical—sit venia verbo—rather than mathematical. As physicians we are convinced, but we may fail to carry conviction into the patient's mind.

Our available criteria are presumptive and retrospective, resting upon information as to the mode of origin of the abarticular symptoms, and upon observation as to their disappearance under treatment, or after the occurrence of an articular outbreak. These are the criteria which, carefully handled, are of most value. The mode of onset

may provide strong presumptive evidence, especially in the absence of any other explanation. A definite and immediate alternation with an acute articular attack possesses yet greater weight of proof, especially if the alternation should be of the repeating type, the dispelled abarticular symptoms returning again after a suppression of the arthritis.

I.

# AFFECTIONS OF THE RESPIRATORY MUCOUS MEM-BRANE: GOUTY LARYNGITIS, TRACHEITIS, BRONCHITIS.

Local gouty manifestations have often been traced to some local irritation. This causation is well illustrated in the mucous membranes. Those membranes suffer most which are either relatively unprotected or liable to definite temporary over-stimulation.

The frequent association between gout and respiratory affections, long noted by physicians, and partly explained by the prevalence of gout and of a variable climate in this country, bears out the rules as to the excessive vulnerability of gouty tissues, and the ready production of gouty manifestations on relatively slight irritation, and as to the predominant nervous type of the symptoms. The genuineness of the gouty relationship of these affections has not often been contested, but the closeness of their association with gout varies, and likewise its type, as will be seen in bronchitis, the chief and most prevalent among them. The affections of the higher air-passages alone afford us some insight into the changes in the mucous membrane.

A gouty laryngitis in the strictest sense, i.e., associated with obvious deposition of urates, sometimes occurs. Reported instances of this kind are rare. Deposits of

urates have been observed by Garrod\* on the arytenoids, by Virchow† on the right vocal cord, by Litten‡ in the crico-arytenoid ligaments and joints, by Norman Moore§ in both vocal cords, and by Brooke in connection with rigidity of the vocal cords.

The occasional occurrence of these changes justifies the inference that, at least in the larynx, where fibrous tissues abound, the condition which we call gouty may be connected with actual deposition of biurate.

Garrod¶ was led to infer the existence of a similar condition and of rigidity of the articulations in a case of inveterate gout, in which partial and then absolute aphonia, finally combined with dysphagia, were observed.

The common form of gouty laryngitis is confined to changes in the mucous membrane, analogous, so far as we know, to the pharyngeal condition described as gouty. Undue congestion is its prominent feature, and with it more or less swelling. The congestion may extend to the vocal cords. The symptoms of hoarseness, irritation, cough, scanty and occasionally blood-stained expectoration, proceed unchecked so long as the cause is not under control. Even climatic treatment, whilst mitigating the trouble, will not always cure it; and it is much intensified by unsuitable atmospheric conditions.

Gouty tracheitis has not been often described as a separate affection, though often associated with gouty laryngitis or with gouty bronchitis. The appearances and the symptoms do not differ from those of ordinary tracheitis, unless, perhaps, in the greater irritation of cough and the more than usually scanty secretion.

<sup>\*</sup> Loc. cit., p. 452. + 'Archiv.,' vol. xliv.

<sup>‡</sup> Virchow's 'Arch.,' vol. lxii., p. 132 (quoted by Duckworth, p. 85).

<sup>§ &#</sup>x27;Pathological Society's Transactions,' xxxiii.

Medical Times and Gazette, 1871 (cf. Rendu, p. 108).

<sup>¶</sup> Loc. cit., p. 452.

The Gouty Bronchial Affections.—So common are the bronchial complications that the gouty connection has been dwelt upon by most writers on diseases of the chest. Laennec, Andral, Stokes,\* Greenhow† all refer to it, as well as do the writers on gout.

Strict evidence of the occurrence of uratic deposits in connection with the bronchi is not forthcoming; but sputa containing uric acid have been described by Lecorché and by Dr. J. W. Moore,<sup>†</sup> among others, and may have been derived from the bronchi, though more probably from the larynx.

The intensity of the bronchitis presents three degrees: acute bronchitis, chronic bronchial catarrh, and mere irritability of the tubes not amounting to bronchitis. Its relation to the gouty symptoms may be direct or vicarious. Thus, bronchitis may accompany the arthritic symptoms, it may replace them in any given case, or it may alternate with them in hereditary transmission. Lastly, its special feature is the presence of a nervous or spasmodic factor.

Acute gouty bronchitis is sometimes extremely severe, and in the subjects of inveterate gout, especially when renal changes have occurred, or in the aged, it may be fraught with danger. As a rule, the urgency of the bronchial symptoms bears an inverse ratio to that of the arthritic, the latter tending to remit with the bronchial exacerbations. Occasionally, however, the bronchitis is part of the fit of gout; but much more often it is either a premonitory affection, abating somewhat suddenly on the advent of the latter, or it breaks out on the abrupt cessation of articular pains. In both cases it is often accompanied

<sup>\*</sup> Cf. 'Diseases of the Chest,' 1837, pp. 84, 90, 91.

<sup>† &#</sup>x27;On Bronchitis and the Morbid Conditions connected with it,' second edition, 1878; also on 'Gouty Bronchitis,' Lancet, 1867.

<sup>‡</sup> Irish Hospital Gazette, July, 1863 (quoted by Duckworth).

with great constitutional disturbance, hepatic derangement, and irregularity of the heart's action.

The dyspnœa is aggravated by the attendant pulmonary congestion, which may be evidenced by the staining of the sputa, and by the conjunction of fine bronchial râles; and emphysema generally underlies the bronchitis of the older subjects, and adds to its gravity.

Subacute gouty bronchitis and chronic gouty bronchitis are proverbially troublesome and obstinate. They belong specially to the phase described as 'goutiness,' occurring more commonly in the intervals than during the arthritic seizures. The state of the mucous membrance, as originally described by Laennec,\* may be inferred from the symptoms, viz., irritative and painful cough, considerable oppression, and a scanty 'pearly' expectoration. 'Dry bronchial catarrh' is the name which he gave to it. Analogous clinical features belong to gouty laryngitis and pharyngitis, and we are led to suspect in the bronchial membrane similar changes to those which may be seen in those situations.

The gouty character of this affection has occasionally been called in question, in spite of the cogent reasons upon which the prevailing opinion is based. Most striking of all are the marked alternations seen in some subjects with arthritic seizures, and the decided relief afforded by treatment capable of controlling the gout. Scarcely less important are, in some cases, the association, in others the alternation, with it of cutaneous eruptions, such as are observed with great frequency in gouty states, and particularly of an urticarial rash, of eczema, or of psoriasis. Habitually the cutaneous and the bronchial symptoms replace each other, but their combination is not uncommon.

<sup>\* &#</sup>x27;Auscultation Méd.,' i., p. 171; 2eme édit.

It is also significant that the tendency to a form of bronchitis indistinguishable from the gouty, and capable of alternating with the characteristic rashes, is apt to be inherited from gouty parents, though articular gout may not evolve. Cases must have occurred in the practice of all physicians who have devoted attention to gout in which bronchitis accompanied the rash in its regular seasonal reappearance in spring and autumn.

Simple irritability of the bronchial membrane is a third degree in which mild gouty influences may take effect. This form belongs mainly to the class of inherited goutiness. The bronchial delicacy of many children, so difficult to explain on any other basis, is probably to be accounted for in this way. The subjects may not develop articular gout until late; they may not present the inveterate type of bronchitis described above; but they are constantly liable to slight bronchial colds, often of short duration, and to laryngeal irritation upon trivial exposure.

The Expectoration in Gouty Bronchitis.—A clinical feature of importance, though not restricted to gouty bronchitis, is the frequent occurrence of Charcot-Leyden crystals.

According to the most recent observations, these are a phosphatic combination of spermin, itself a derivative of nuclein, and they are intimately associated with a proliferation of leucocytes. This peculiarity of the sputum might by some be regarded as an argument in favour of the connection of this form of bronchitis with gout.

Gouty Asthma.—Cases have frequently been observed in which genuine gouty attacks have alternated with equally genuine asthmatic seizures. Even those authorities who, with Germain Sée, are sceptical as to the alleged causation, admit in the majority of instances that there is a gouty form of asthma.

A larger group is that of patients who develop the

respiratory neurosis early, and, after a long asthmatic history, develop articular gout.

In a third group are included the hereditary cases, in which asthma in the progeny seems to take the place of the articular gout of the parent. A similar relationship has sometimes been reported between hay asthma and gout: Noel Guéneau de Mussy has insisted upon this. Trousseau, Murchison, Garrod, Durand-Fardel, Lecorché, Duckworth, have all recognised the close association of gout and nervous asthma.

Laennec himself noted retrocedent gout as a cause of asthma,\* and Trousseau ('Clin. Méd.,' ii., p. 377) gives a case of a child, aged five, a sufferer from asthma and emphysema, who at this age had a distinct attack of gout, and while thus affected was free from asthma.\*

As to the association, with asthma, of skin affections in appearance identical with those which occur in the gouty state, we have, according to Wilson Fox,† the testimony of Trousseau,‡ of Andral,§ of Hyde Salter, and others. Von Waldenburg|| is also quoted by Wilson Fox as dwelling on this association, and referring to its alternation with the attacks, applying to this form the name 'asthma herpetiforme.' Trousseau had previously insisted that the 'herpetic constitution' ('dartres,' gout, rheumatism, and hæmorrhoids) might lead up to asthma.

The so-called uræmic asthma is an entirely distinct affection, and need not be considered in this connection.

Gouty Pulmonary Emphysema. — Secondary emphysema is an inevitable result of a long continuance of gouty

<sup>\*</sup> These references are given by Wilson Fox, 'A Treatise on Diseases of the Lungs and Pleura,' edited by Sidney Coupland, M.D., F.R.C.P., 1891, p. 54.

<sup>†</sup> Loc. cit., p. 54.

<sup>‡ &#</sup>x27;Clin. Méd.,' ii., p. 399.

<sup>§</sup> Ibid., iii., p. 258.

<sup>| &#</sup>x27;Locale Behandlung,' etc., p. 84.

bronchitis and asthma. A primary form has also been described, occurring independently of the mechanical operation of bronchitis, and traceable to the general influence of gouty malnutrition. Sufficient reference has been made to it elsewhere (cf. p. 134).

Gouty Pulmonary Congestion and Hamoptysis.—Lecorché,\* who devotes special remarks to these events, draws attention to the great liability to them inherent to the gouty state by reason of the age and to the coexisting organic lesions, cardiac, vascular, and renal. Over and above merely secondary congestions, he believes in the existence of a tendency to congestion peculiar to the gouty state. The seat of the congestion, usually basic, may also be localized at the apex. He refers to the observation of E. Collin,† who professes to recognise it by the peculiarity of its râles.

Huchard<sup>‡</sup> has also dealt exhaustively with this, and reports cases of severe recurrent hæmoptysis in confirmed gouty subjects, some of whom Barth, Andral, and Gendrin had regarded as phthisical.§ These cases probably belong to the same category as those described by Sir A. Clark, to which we have already referred (cf. p. 130).

A gouty pneumonia was admitted by Musgrave and by ancient authorities, as well as a gouty pleurisy. Lecorché, who does not recognise the latter, admits the pneumonia, and relates two cases of his own and one by Brissaud in which a definite alternation with arthritic gout could be traced. English authors have not recorded cases.

<sup>\*</sup> Loc. cit.. p. 319.

<sup>† &#</sup>x27;Du Diagnostic de la Congestion Pulmonaire de Nature Arthritique et de son Traitement,' 1877.

<sup>‡ &#</sup>x27;Congrès de l'Assoc. Franç. pour l'Avancement des Sciences,' 1883.

<sup>§</sup> Lecorché, loc. cit., p. 322.

<sup>|</sup> Ibid., p. 324.

# II.

THE MUCOUS MEMBRANE OF THE ALIMENTARY TRACT.
—GOUTY AFFECTIONS OF THE MOUTH, FAUCES,
STOMACH, AND INTESTINE.

The tongue is generally moist, and, according to Dickinson,\* often stippled in acute as well as in chronic gout. It sometimes presents the characteristic appearance of glossitis migrans or of leucoplakia. In other instances it may be unduly red and thinly covered with epithelium, especially in gouty dyspeptics.

Heat and burning sensations, or severe neuralgic darting pains, are often part of a gouty tic douloureux. Discomfort, or even severe pain, may, however, affect the organ independently in gouty subjects, and sometimes even, according to Paget,† give a false alarm of cancer.

Gouty Pharyngitis.—The best opportunity for a study of the gouty influences on mucous membranes is afforded by the pharynx. In the previous history of gout or goutiness, in the uselessness of topical applications and of the usual treatment, and in the rapid relief obtained by a treatment directed to the gout, we possess strong arguments for the view that the throat is liable to strictly gouty affections. The characteristic appearances are a considerable and somewhat dusky redness of the arches and velum palati, of the uvula, and of the pharynx. The entire membrane, but particularly that covering the uvula, is swollen, and apparently cedematous, the fine detail of its surface being obscured. The uvula is often much increased in size, and at its extremity the swollen mucous membrane is apt to be drawn out into a fine appendix. The

<sup>\*</sup> Lumleian Lectures, 1888, p. 36.

<sup>†</sup> Quoted by Duckworth, loc. cit., p. 87.

pharynx may have been previously granular, and will not then present the same degree of smoothness of surface. It may be partly coated with mucous discharge, but, as a rule, the appearances mentioned are the most striking.

Tonsillitis of a gouty character also occurs. In N. Guéneau de Mussy's + case the pharyngeal follicles discharged carbonate and urate of lime.

Gouty Affections of the Stomach.—Sydenham's observation that gastric disturbance, one of the most frequent prodromata of acute gout, became more constant and more severe with the progress of the affection, has been confirmed by all later authorities, and a close connection has been universally admitted to exist between gout and peculiar gastric irritability and intolerance.

Aggravated dyspepsia is also one of the most prominent symptoms of 'goutiness' in those who, inheriting the predisposition, have not developed articular gout. Garrod gives it a place among the abarticular manifestations of gout, and attributes it to the impurity of the blood arising from the impaired state of the kidneys.

The evidence upon which the alleged gouty nature of the gastric complications has been based is entirely clinical. Hitherto no uratic deposits have been recorded as occurring in the stomach, neither has it been possible to trace any definite alteration in the mucous membrane, beyond trifling changes in its surface and the practically inconclusive occurrence of congestion.

On the other hand, the *symptoms* are considerable, and sometimes grave. They involve acute derangements of all the functions of the organs, secretory, motor, and sensory. Vomiting and retching are often severe and obstinate, and great flatulent distension and persistent hiccough and gastralgia, associated with cramp, are also observed.

<sup>\*</sup> Union Méd., No. 18, 1856 (quoted by Duckworth, loc. cit., p. 86).

Since all these symptoms frequently originate from causes unconnected with gout, proofs of their gouty nature must be sought in the clinical history and in the general features of the case. Gout or goutiness has to be diagnosed, and the gouty nature of the symptoms which are not distinctive may then be inferred. In the absence of any articular manifestations, the inference is a large one, and has called forth much scepticism, such as that of Brinton and Sir Thomas Watson.\* In other cases a strong presumption may be based upon the march of the symptoms. The connection between the gastric and the articular manifestations may be one of concomitance, as in the onset of the acute arthritis; or of alternation, as in the case recorded by Sir A. Garrod; or of metastasis. These relations may be regarded as the clinical tests of the gouty nature of visceral attacks in general.

Of much diagnostic value is the strong nervous element perceptible in the history of many cases. The gastric attack is commonly induced by severe mental strain or shock, and may be immediately followed by an articular seizure. This factitious causation under avoidable circumstances is also seen in some patients whose articular symptoms may originate in this way, without the gastric prodroma.

The chief clinical forms of gouty stomach affections are the chronic dyspeptic, the chronic catarrhal, the gastralgic, and the metastatic variety.

Gouty dyspepsia, a chronic and inveterate ailment, is usually coupled with a peculiar intolerance for certain articles of diet. There is commonly much acidity, with or without acid eructations, and flatulence. It is apt to coexist with the gouty state.

Chronic gastric catarrh is also a complication of advanced

gout, and is aggravated by the cachexia. It is known by the characteristic daily or periodic vomitings of stringy mucus or of clear fluid.

The chronic gastralgic varieties, as pointed out by Rendu, are more commonly observed in inherited goutiness, long preceding the articular attacks, the advent of which may be their cure. Remarkable instances of the rapid amendment of a long-standing painful dyspepsia on the development of articular gout have been reported by Ebstein, Rendu, and others.

It may happen that after the cessation of a long-established recurrence of gouty attacks gastralgic dyspepsia may supervene. Treatment appropriate to the gout will usually be followed by improvement.

Gouty metastatic gastritis belongs to the most severe clinical type of gouty retrocedence. Whether this name is accurately descriptive is an open question, little being known concerning the anatomical changes.\* The frequency of this affection is less than reported by former observers, and there is much probability in Duckworth's suggestion that before Heberden's time a proportion of the fatal cases must have been instances of angina pectoris.

Gouty Gastro-intestinal Affections.—The intense irritability or intolerance of the goutily affected membranes to relatively slight irritation is nowhere better exemplified than in the gastro-intestinal tract. Vomiting, gastralgia, colic, and diarrhæa, sometimes violent and accompanied with depression, are apt to occur on relatively trifling provocation. Here, again, as in bronchitis, the relief afforded to the disturbed membrane by some gouty out-

<sup>\*</sup> Duckworth (*loc. cit.*, p. 89), however, gives a case in which some pathological change was found, and refers to another recorded by Moxon ('Transactions of the Pathological Society,' 1870), which presented intense congestion, submucous hæmorrhages, and adherent pellicles of lymph.

break elsewhere is almost conclusive evidence of a strongly gouty element in the symptoms described.

The prevalence of dyspepsia and irritable bowels is so great also among those who present very different clinical family histories and constitutions, that it is difficult to demonstrate the gouty nature of the more chronic and trivial forms of gastric or intestinal disturbance in the individual case unless light should be thrown upon it by a gouty record, or by the local vestiges of past attacks.

In the metastatic variety all doubt of this kind is practically removed, so sudden and striking is the transference of suffering from the joints to the mucous membrane. The question whether the metastasis is a purely nervous phenomenon, or may assume the proportions of a definite lesion, is one difficulty to set at rest, although in favour of the latter view we derive strong analogies from the visible changes in the pharyngeal membrane, and from those obtained by means of the cystoscope, as well as from an inspection of the discharge from the bladder in gouty cystitis.

Gouty Enteritis.—As with gouty gastritis, it is difficult, where so many other influences may be at work, to prove that the affection in a given case is specifically gouty. It may be well to define at once clearly the varieties which have been described. Gastro-enteritis may be set up by irritants of various kinds, and the occurrence of irritation is specially frequent in gout, whether owing to excess or, as in inherited delicacy, to undue susceptibility. Attacks due to indigestion are the most common. A small group of cases of enteritis, more strictly so called, has been connected with gout itself as a most likely cause, and Dr. Haig has advocated the use of salicylates in its treatment. Sir Dyce Duckworth\* is also a believer in the existence

<sup>\*</sup> Loc. cit., p. 291.

of a gouty enteritis, of which he recognises a spasmodic and a catarrhal form—the first apt to be complicated with constipation, the second with diarrhœa and vomiting. The writer has witnessed a remarkable case of the second type in an alcoholic and albuminuric patient. The severity of the symptoms was alarming, but the patient recovered; and two mild attacks of gout in the toe occurred at intervals of a few days.

The fact that the 'arthritic colic' of Musgrave, which Sir Dyce Duckworth regards as having often been lead-colic from cider-drinking, is so much less commonly seen in our times, finds the same ready explanation as the reduced frequency of gouty gastritis. The organs are less tried than they were in days of less careful living. Above all, abdominal diagnosis has made giant strides. To say nothing of lead-colic itself, biliary colic, floating kidney, appendicitis, and ovarian affections have divided between them the major part of the previous domain of gouty gastro-enteritis.

#### III.

GOUTY AFFECTIONS OF THE URO-GENITAL MUCOUS MEMBRANE: AND OF THE ORGANS OF REPRO-DUCTION.

Gouty 'Irritable Bladder.'—The bladder troubles often diagnosed as gouty are probably swelled by those merely depending upon senility, with its tendency to atony, sedimentation, sacculation, prostatic enlargement, retention, and catarrh. Any of these might conceivably act as the exciting cause of a superadded gouty affection. At any rate, the condition known as irritable bladder is common in the gouty, and, as suggested by Todd,\* bladder

<sup>\*</sup> Cf. Todd, 'Clinical Lectures on certain Diseases of the Urinary Organs,' 1857.

affections are not less likely to occur under the influence of gout than bronchitis or gastritis.

The irritant to the membrane is usually the urine itself, through its excessive acidity, or the presence within it of sharp crystals of uric acid or of calcium oxalate. The urethritis stated to occur sometimes towards the end of a gouty arthritis bears the same interpretation.

Gouty Urethritis and Cystitis.—Here, again, we cannot lose sight of the influence of age as affecting the question as to a strictly gouty causation.

That the bladder is liable to a distinct gouty catarrh has been asserted on the strength of instances of its metastatic implication in the course of an arthritic attack, or on the abrupt cessation of a severe gouty eczema. Sir Dyce Duckworth\* describes such acute symptoms as sudden onset of pain, hæmaturia, ardor urinæ, mucopurulent sediment in a scanty, high-coloured urine, often persistence of the acute stage for days, and of the chronic condition for weeks. He also points to the occasional concomitant or immediately ensuing affection of the heart, or some other organ, before the gout may return to the joints, as a proof of the gouty nature of the cystitis.

Urethritis may also be metastatic, according to the same authority, and accompanied with puriform discharge and scalding, such as to cast doubt at first on the diagnosis.

Spontaneous hamorrhage from the bladder, independently of gravel or stone, was regarded by Todd as capable of a gouty origin.

Gouty Orchitis.—This is recognised by some surgeons of experience as a distinct affection traceable to gout, and amenable to its treatment. My colleague, Mr. Bennett, informs me that he has seen it repeatedly. It is associated

with effusion into the tunica vaginalis, and implicates the entire organ. Debout d'Estrées\* has observed its occurrence without effusion. Parotitis, according to Duckworth, though it may occur from gout, has not been recorded in connection with gouty orchitis.

The Ovary and the Uterus in Relation to Gout.—Looking at the hereditary feature of gout, we might regard its incidence on the ovary as not improbable. The existence of ovarian gout was formerly recognised, but is not now believed in by the majority of gynæcologists, and would be difficult to prove, though a gouty origin would not be easily excluded in cases of unexplained ovaritis occurring in gouty subjects at the gouty age.†

Again, the apparent probability of a liability of the uterus to gout is obvious. The immunity of so important a mucous membrane as the uterine, and of one reacting in so marked a degree to constitutional states, and fulfilling, moreover, an emunctory function in relation to the blood, would be matter for surprise in contrast with the liability of all other mucous membranes, but for its relative freedom from exposure to irritation. Uterine gout was formerly much dwelt upon.

A gouty uterine catarrh was recognised by Storck and Stoll, and much more recently by Sir Spencer Wells‡ and by N. Guéneau de Mussy. The latter traced in some cases an alternation between the uterine catarrh and

<sup>\*</sup> Quoted by Duckworth (loc. cit., p. 113).

<sup>†</sup> Duckworth (*loc. cit.*, p. 277) quotes Sir W. Priestley's opinion, that 'women of gouty heritage are more apt than others to suffer from chronic metritis, chronic capsular and interstitial ovaritis, and menorrhagia.'

<sup>‡ &#</sup>x27;I have known some cases, and heard of many others, where the females of the family, the male members of which suffered from ordinary attacks of gout, have been subject to a kind of uterine catarrh, the uterine discharge being very thick and irritating, or abundant and watery' (loc. cit., p. 166).

bronchitis and eczema, and lays weight upon the circumstance that the catarrh is often accompanied with vulvar eczema and pruritus.

Rendu, who discusses these possibilities at some length, does not venture to assert the existence of a distinct 'uterine gout,' but is a firm believer in a constitutional element at the root of some forms of catarrh and of menorrhagia. The present attitude of gynæcologists is one of scepticism as to the alleged connection.

#### CHAPTER XXV.

# THE LIVER AND THE KIDNEY IN GOUT.

# THE GOUTY AFFECTIONS OF THE LIVER.

Gouty GLYCOSURIA may be regarded as the result of hepatic derangement, and a long chapter might be devoted to this subject alone; yet this is but one form of the gouty hepatic disorders. Next to the frequency of minor disturbances attributable, or at any rate attributed, to the liver, the most striking fact is the rarity, nay, the absence, of any serious organic affection traceable to the disease. It was long ago pointed out by Garrod that the liver is not the seat of any uratic deposits, and does not undergo structural changes differing from those which are observed in non-gouty subjects.

A slight hepatic congestion commonly accompanies the acute gouty attack; this has been noted by most observers. Again, recurring or habitual functional biliary irregularities are the prominent feature in the clinical history of some sufferers from goutiness. Neither this nor the more severe forms of hepatic disturbance presently to be mentioned lead, however, so far as we know, to any perceptible organic change.

Secondary hepatic disturbances in gout are of every-day occurrence. The most frequent and least dangerous are transient attacks in which the liver is rather sinned against than sinning. Many of these, however, are truly

gastric, the outcome of real excess in the case of the plethoric and non-dyspeptic subjects, or of relative excess or imprudence in those of weak stomach, or, lastly, of reflex indigestion in the high-strung nervous persons in whom goutiness is usually inherited.

'Gout in the Liver.'—A much more serious condition is sometimes observed. The liver appears to bear the brunt of the gouty process, whilst all other local manifestations are in abeyance. The hepatic functions are radically disordered; nutrition suffers severely, and the patient's weakness, emaciation, muddy pallor or subicteric sallowness and cachectic look, may be such as to create serious alarm, or even to raise a suspicion of the presence of carcinoma. The symptoms may continue unabated for weeks, when under appropriate treatment perfect health may be restored.

The descriptive name 'gout in the liver' may be a pure metaphor. We possess no strict evidence of the gouty nature of the attack; it may be merely an intercurrent phenomenon in a gouty clinical history. Indeed, its pathology itself is obscure. Most probably the grave derangement in the function of the liver-cells is the outcome of a subacute and pervading catarrh of the intrahepatic biliary system, which may lead to a sub-acute parenchymatous hepatitis. We are familiar with similar gouty processes in the respiratory, the genito-urinary, as well as in the entire length of the alimentary mucous tract. The implication of the parenchyma would, according to this view, own a simple and common mechanism, and would derive its specially serious features from the structural peculiarities of the organ. This remarkable affection is met with in the subjects of irregular, or imperfectly arthritic, gout, who are often the inheritors of a gouty tendency, and perhaps more specially in women.

Metastasis to the Liver.—The metastasis of acute gout to the liver has not been dwelt upon by modern authorities. Putting aside biliary colic, no symptoms probably occur sufficiently severe to excite special attention. It is difficult to say to what extent the liver may suffer directly under the influence of the acute gouty state. Rendu believes in gouty paroxysmal congestions of the organ, and gives the case of a lady (the subject of asthma) who was liable to severe hepatic crises, apparently congestive, with considerable increase in the size of the liver, but without any vomiting or the slightest evidence of gallstone. The attacks were excited by indigestion, by the onset of the catamenia, and particularly by moral influences, and were liable to alternate with attacks of diarrhœa, which brought relief rather than distress, and a diminution in the hepatic swelling.

The Biliary System and Gall-stones in Gout.— The immunity of the liver in gout from any structural lesions is in itself an important and suggestive fact, especially since a great proportion of those changes which occur are connected with the presence of biliary sedimentation or gall-stones. The relation of biliary lithiasis to gout has been much debated, and from an early date. Rendu,\* who mentions the observations of Hoffmann, Morgagni, Portal, and others, gives the evidence collected by Senac of Vichy, who found that, among 166 cases of biliary lithiasis, 95 had gout or an inherited tendency to it. Bouchard likewise found that gout in the parents occurred in 30 per cent., and rheumatism in 43 per cent., of the cases.

Rendu suggests that the connection with gout may have often been overlooked because biliary colic is a disease of the younger adult, gout coming on later in life,

<sup>\*</sup> Loc. cit., p. 144.

when gall-stones tend to acquire considerable size and to excite less spasm. Murchison had dwelt upon the frequency of jaundice in gout, independently of biliary colic, and given instances of the occurrence, under the influence of heredity, of congestive jaundice in connection with gout, in several members of the same family.

#### GOUTY AFFECTIONS OF THE KIDNEY.

There are few clinical facts to note in relation to the kidney; they refer mainly to the varying characters of the secretion, including temporary or permanent albuminuria, which have been elsewhere described, and to the insidious progress of the interstitial changes.

The Gouty Kidney.—With the exception of pain arising from renal calculus or gravel, renal symptoms do not usually excite the patient's notice. There is nothing abrupt in the development of the chronic kidney affection, and acute tubal nephritis is exceptional. The first indication of renal trouble observed by the patient is the increased frequency and abundance of micturition; that for which the physician will look is the increased tension in the arterial system.

The severity and the duration of the chronic affection vary widely. A rapidly fatal course is the exception. The rule is rather for the cases to progress slowly and last long. Intercurrent affections, and especially cerebral hæmorrhage or pulmonary congestion, or the ultimate cardio-vascular consequences of Bright's disease, close the scene more commonly than acute uræmia.

Renal Congestive Gouty Attacks.—The kidney might have been regarded as not the least likely among organs to suffer from acute and alternating gouty attacks; but of occurrences of this kind nothing definite is known.

Charcot, however, has observed the signs and symptoms of temporary renal congestion, viz., deep-seated lancinating pains in the loins, slight albuminuria, and even hæmaturia, not necessarily bound up with the passage of gravel, and therefore capable of bearing the interpretation in question.\*

Temporary albuminuria is well known to be a frequent, though not constant, accompaniment of the acute attack, disappearing entirely with its cessation. Lecorché has found its occurrence to coincide with the renewed excretion of the uric acid on the third or fourth day, after which it soon disappears, as the amount of uric acid excreted lessens again. An occasional transient albuminuria, without obvious or definite provocation, is also observed in gouty subjects who may remain permanently free from renal disease. This is probably in most cases the result of faulty digestion or assimilation or of undue acidity. We possess no evidence in support of the view that functional or cyclic albuminuria is more common in gouty subjects than in others.

Permanent albuminuria of slight degree has been shown by Garrod to be a frequent occurrence in confirmed gout. It is highly suggestive of renal disease. Nevertheless, the irritation due to the not infrequent co-existence of oxaluria should not be forgotten as a possible explanation in some cases of recurring albuminuria and hæmaturia.

Ephemeral glycosuria may accompany the acute attack. The frequent association of glycosuria with chronic gout need not be insisted on at this place; glycosuria and diabetes will be further considered under the heading of Treatment.

<sup>\*</sup> Cf. Rendu, loc. cit., p. 127.

# CHAPTER XXVI.

# THE HEART AND BLOODVESSELS IN GOUT.

# THE GOUTY HEART AFFECTIONS.

The 'Gouty Heart.'—It has already been hinted that it is difficult to separate the 'gouty heart' from some other forms of chronic disease as a specially distinct anatomical quantity, although lesions of the coronary arteries and their consequences are conspicuously common in gout. On the other hand, the term is clinically appropriate when applied to the symptoms and aspects of the functional cardiac derangements peculiar to gouty subjects.

Distinct cardiac features belong to granular kidney disease: those of hypertrophy of the left ventricle, such as powerful cardiac impulse, a displaced and forcible apex beat, an increased area of dulness, and loudness of the first sound, etc.; and those of peripheral resistance and high blood-pressure, viz., sustained and hard pulse, exaggerated loudness of the second sound, reduplication, with loudness, of the first sound at the apex, and ultimately a thickened and rigid condition of the arterial wall. Subsequent failure and dilatation of the hypertrophied heart, with its greatly increased dulness, tumultuous and rapid action, overcharged pulmonary and venous system, are also easily identified.

Again, atheromatous degeneration of the coronary arteries, and the resulting fatty degeneration of the heart-wall, pre-

sent well-known symptoms and signs. None of these cardio-vascular symptoms, common as they are in gout, are exclusive results or features of the affection. They should not be included under the term 'gouty heart' in its clinical acceptation.

When these major complications induced by kidney disease in inveterate gout have been deducted, there remains a large set of heart symptoms independent of coarse organic lesion, in which we can trace the operation of the special factors of gout. Dr. Mitchell Bruce has devoted to their description a valuable article in the *Practitioner*;\* and Dr. Balfour refers to them in his recent work. The paroxysmal character of these changes, coupled with their capacity for relief by appropriate treatment, shows them to be mainly *functional*. The minute structural changes which may underlie them do not admit of demonstration, any more than those due to gouty malnutrition in the other tissues.

In the functional peculiarities of the gouty heart we recognise, as elsewhere, irritability and diminished resistance, especially in connection with innervation. The gouty heart is typically a nervous heart.

Irregularity is generally the first degree of the irritation and excitability. In itself this is not a gouty symptom. The irregular and intermittent pulse of the middle-aged or elderly subject is often, strictly speaking, an evidence of his gouty dyspepsia. The arythmia may sometimes become extreme, and may be accompanied with distressing sensations.

Unnatural rapidity may be associated with the consciousness of heart-hurry, or palpitation; or it may be unconnected with any subjective feelings. The overacting and thumping heart is generally a 'conscious' one.

<sup>\*</sup> Cf. Practitioner, January, 1895.

Bradycardia, or unnatural slowing, a permanent anomaly in some conditions, is often in gout or goutiness of temporary duration, and apt, like tachycardia, to occur on the sudden retrocession of the articular symptoms. More commonly its onset is unexplained, and should then suggest the possible influence of a latent gouty state.

Why such opposite conditions should be capable of this alleged uniform derivation is a problem as obscure as everything relating to cardiac neuroses. Individual peculiarity is nowhere more striking than in connection with the character of cardiac action. Quite apart from gout, some subjects present an acceleration, others a slowing of the heart's rhythm under mental excitement; and visceral stimuli probably take similar effect. Nay, the same heart may at different times be liable to hurry and palpitation, or to distressing slowness and feebleness of action.

Painful heart affections also belong to the group of functional disorders of the gouty heart. Their importance is great in proportion to their resemblance with true angina, itself a too frequent result of gout, to the difficulty of a safe diagnosis, to the opposite indications of treatment, and to the contrast in the prognosis of the two conditions. In its fully-developed form the painful affection has received the name of pseudo-angina. Its outward symptomatic identity with angina is sometimes so great that we may question the propriety of the qualification 'false'; at any rate, in respect of the pain and of the cardiac distress. The chief difference lies in the causation, not in the symptoms. The same agony of pain and of suffocation, the same irradiation down the arm, the same feeling of arrest of breath and circulation, the same gastric complications, may be present in both; but their significance is totally different. Perhaps the chief distinction between

the more severe functional seizures and the fits of real angina resides in the patient's innermost feelings: dread of death in the one case, consciousness of dying in the other. The age of the patient might be of greater diagnostic value were it not that the period for confirmed gout is also that for angina; moreover, the immunity from fatal angina is not absolute even in early adult life, though the cases observed are undoubtedly rare.

Well-authenticated cases are on record in which grave attacks supervened immediately after the retrocession of articular symptoms, and were clearly connected with gout. Fortunately, the type of the functional affection is not usually pure, and most cases may be described as anginoid rather than anginal. Not only may we miss the symptom of meditatio mortis, but there may be comparatively less of faintness than of cardiac and irradiated pain, whilst the flatulency and gastric disturbance may be more prominent features. Again, in the history of the attack indigestion often plays a more conspicuous part than is usual in Heberden's disease.

The Minor Cardio-vascular Symptoms of Goutiness.—Any of the symptoms described may occur in immediate and alternating relation with articular seizures, or they may appear on the scene quite independently, even in those who merely inherit a tendency to gout. A practical acquaintance with instances of the same direct association explains the view\* taken by former physicians, that most of the cardio-vascular neuroses which are so common in young females were gouty manifestations. One of the most striking among them—Graves's disease—may undoubtedly sometimes occur in gouty families. Much more often no such connection can be traced. The same remark applies to the pseudo-anginal seizures of young

women, and to various other neurotic conditions, which, for want of some better explanation, are usually classed as hysterical.

The frequency with which various minor derangements of the cardio-vascular functions occur in goutiness leaves us in little doubt as to their being related to the latter. Localized excessive arterial pulsations, peripheral ischæmiæ and hyperæmiæ, permanent dilatations of peripheral vascular districts—as seen in the red line at the root of the nails—angio-neurotic ædema and urticarial rashes have all been described in this connection.

The articular affection itself has been referred by some to a paroxysmal venous dilatation, and by Owen Rees to a 'dilatation of the capillaries.'

#### THE GOUTY AFFECTIONS OF VEINS.

Phlebitis,\* more painful in some cases than in others, is always an important affection needing patience on the part of the sufferer and prudence in the physician. Gouty phlebitis differs from some other forms in the more abiding character of its cause and in its marked tendency to recurrence, which necessitates the avoidance of all circumstances likely to produce a relapse. The dangers of any mechanical disturbance of the limb—the lower extremity is much more frequently affected than the upper—and of any general vascular excitement, are particularly to be thought of during the stage of softening of the clot, when its more friable portions are liable to be washed into the venous current in sufficient quantity to lead to pulmonary embolic thrombosis. It is not impossible that some of the minute débris

<sup>\*</sup> Cf. Sir James Paget, 'St. Bartholomew's Hospital Reports,' vol. iii., 1886; Sir Prescott Hewett, 'Clin. Soc. Trans.,' vol. vi., 1863; Dr. Tuckwell, 'St. Bartholomew's Hospital Reports,' vol. x., 1874, quoted by Duckworth, loc. cit., p. 309.

may gain gradual access to the circulation, without any worse results than an occasional rigor with temporary elevation of temperature. Some cases of phlebitis are specially inveterate. The migratory cedema affecting in succession one limb after another, and the lungs themselves, is not commonly seen in gout. On the other hand, a recurrence in the same limb is frequently observed. Persistence of cedema for long periods is another characteristic of gouty phlebitis; but individual cases vary much in this respect.

Men, being more liable to gout, are also more often the sufferers from this form of phlebitis.

Phlegmasia Alba Dolens.—This distressing affection may be regarded as an ordinary phlebitis on a large scale, involving specially the deeper veins, and leading to an unusually firm cedema with much tenderness and pain; there is still much mystery connected with its pathology. Whether primarily—and this would seem extremely probable—or as a result of the great pressure, the lymphatics of the parts are disabled and absorption almost completely suspended; hence the long duration of such cases.

Phlegmasia dolens, so prominently connected with the puerperal states, is also an affection of the male, and particularly of the gouty male. Striking cases, observed by Dr. Edward Liveing, are given by Sir Dyce Duckworth (loc. cit., p. 310). A hereditary tendency independent of gout is a well known peculiarity of this disease. Sir C. Locock's instance of four daughters suffering from phlegmasia, whose father also had phlebitis, is often quoted. But there is probably a special tendency to this transmission when gout is the pathological heritage.

Gouty phlebitis is specially selected by Sir James Paget\* as a support for the view that new developments are being

<sup>\* &#</sup>x27;Clinical Lectures and Essays.'

evolved in our diseases. So disabling, disfiguring, and tediously prolonged an affection as phlebitis could not have escaped notice, and if noticed could not have been ignored by our predecessors; the absence of records relating to it would suggest that it was not, at any rate, of common occurrence.

The well-known frequency of gouty phlebitis enables a diagnosis of gout to be often made where an otherwise unexplained phlebitis suddenly develops in an elderly patient.

The question as to the possible connection between the acute lesions of gout and a local 'capillary phlebitis' (Owen Rees) is discussed elsewhere.

Hamorrhoids are an occasional trouble with gouty patients, and sometimes need very judicious management. Nothing leads us to suspect that any gouty peculiarity attaches to this form of complaint, nor to its mode of causation; and its treatment should be carried out on generally approved principles.

Varicose veins, the production of which is so largely influenced by the state of the portal circulation, and so directly favoured by a plethora of fluids, are apt to be observed in the gouty, particularly in the florid subjects of full habit, and in those with a tendency to obesity and relative cardiac inadequacy. Its occurrence in those whose gout is brought about by beer is well known to every practitioner, and is very largely seen among the poorer class of gouty subjects in London.

# CHAPTER XXVII.

# THE CUTANEOUS SYSTEM AND THE ORGANS OF SPECIAL SENSE.

# THE SKIN IN GOUT AND IN GOUTINESS.

The intimate connection of the skin with the nervous system, which is so largely implicated in gout, adds much importance to its clinical study. Due regard to this association is of the greatest practical use in the diagnosis and in the treatment of gout, as well as of cutaneous ailments. And, again, it warrants us in attributing to the skin, as a department of the nervous system, some share in determining a liability to gout, though the much larger share belongs to the latter. Those conditions which tend to render the skin delicate and susceptible contribute also to establish the liability, whilst in gout itself the cutaneous delicacy is largely responsible, as a determining cause for the onset of various complications, more particularly of the catarrhs.

That the majority of the subjects of acquired gout should possess a smooth and delicate skin may be simply due to the greater frequency of gout among the non-labouring classes. Gout is not restricted to any one type of constitution or of skin; and with special regard to articular gout, it would be impossible to establish a parallel between peculiarities of the skin and of the joints, although

the delicacy of the skin may often be taken as a gauge of the vulnerability of the system at large. More perhaps than any other tissue the skin tells us of the constitution. In the vulnerability often coinciding with a thin skin the lymphatic system and the nervous system are closely concerned. It might be said that the lymphatic delicacy was more prominent in the scrofulous subjects, the nervous more so in the gouty. In the latter we find the great neuro-vascular reactions—the nerve storms—not cerebral only, as in asthenic gout with irritability, but sympathetic, leading to some of the irregularities of gout, and neuralgic, particularly in the asthenic cases subject to gouty neuralgia. The gouty skin affections are also largely under the influence of the nervous system.

Whilst it is difficult to say how far a delicate skin may influence the liability to gout, as to the influence of gout in promoting cutaneous delicacy there is not any doubt. The longer gout lasts, the more marked is this result, and it is apt to be most marked in the offspring, who frequently suffer early from psoriasis, eczema, urticaria, or other affections, and in this way display almost from infancy their constitutional bias.

The peculiarities of the skin and cutaneous appendages commonly observed in the subjects of acquired and of inherited gout need not be described at length. Smoothness and softness of skin are most marked in the subjects of tophaceous and of crippling gout, together with some atrophy, but they are not limited to these types. The opposite condition of harshness and of dryness belongs to other cases, but particularly to a large group of those who inherit goutiness, and of the sufferers from psoriasis derived from gouty inheritance.

The skin of the average gouty subject acts freely under stimulation, and often suffers as a result of the excess and irritating quality of the perspiration.\* During intervals of rest it is less active and drier than in non-gouty subjects.

Sir A. Garrod+ derived the conclusion from an analysis of the perspiration obtained at a Turkish bath from a patient with inveterate gout, that the healthy skin is not capable of eliminating uric acid, even when in excess in the blood. Urea and oxalate of lime were found in the secretion, but no trace of uric acid. He also refers to other observations, and to Charcot's statement that in uræmia, as in cholera, urea, but no uric acid, can be traced in the powdery deposit sometimes found at the surface of the skin. These observations cast considerable doubt on earlier statements as to the occurrence of uric acid as an excretion from the skin. Some of these relate to the contents of the serum from gouty eczema. Golding Bird (1856) believed that he had found urate of soda in the secretion from a case of this kind. Gigot Suard‡ discovered urates in the vesicles of eczema and of pemphigus in a gouty subject. The same observer has attempted to give an experimental proof of the local influence of uricacidæmia upon the skin by the ingestion of uric acid. In the case of a young girl, after fifteen daily doses of 10 centigrammes of uric acid, he observed a few pustules of ecthyma on the hands and face.

Rendu draws attention to the occurrence of acne, boils, and carbuncles as an antecedent, as an alternation, or as a sequel of the gouty attack, in connection with the possibility of a local determination of uric acid to the skin.

The nails become sooner or later characteristic in their thinness and brittleness, and in the longitudinal striation

<sup>\*</sup> The presence of urates in the sweat, although denied by Garrod and by Duckworth, is asserted by Drs. Meldon and Tichborne (Brit. Med. Journ., November 19, 1887, p. 1097, quoted by Duckworth), who give a method for their recognition.

<sup>†</sup> Loc. cit., p. 118.

<sup>‡</sup> Quoted by Rendu, loc. cit., p. 136.

which they almost invariably present. Sometimes transverse striation and pitting are observed.

The teeth have been described as strong and enduring in those who develop gout, less so in the heirs to it.

An abundant growth of hair in early life, with early onset of baldness, is mentioned among the peculiarities connected with a gouty constitution. Early grayness has also been regarded as common in those inclined to gout. What foundation may exist for this belief appears doubtful, having regard to the frequent persistence of a full supply of hair throughout a long life of recurring gouty attacks. Probably, as in the case of early decay of the teeth, some constitutional delicacy or circumstance not connected with gout is the determining agent.

#### THE URATIC CUTANEOUS AFFECTIONS.

The liability of the skin to gouty influence is proved to demonstration by occurrence of deposits within it. The subcutaneous tophi and uratic infiltrations need not be again described (cf. p. 121).

On the strength of this obvious fact, some observers have endeavoured to prove the uratic nature of cutaneous inflammations occurring in gout, and particularly of eczema.

#### THE 'GOUTY' SKIN AFFECTIONS.

Although the attempt to trace uric acid in eczema has failed, the close connection of this and of other skin affections with gout is established by the clinical tests set forth in connection with visceral gout, and with a definiteness not attainable in the case of inflammation of deep-seated membranes. Alternation with the arthritic attacks is a very marked feature, and alternation in inheritance

is often observed. A knowledge of this fact often enables the physician to diagnose goutiness before it has found any further expression. Bazin founded upon it his well-known group of 'arthritic' affections of the skin, and French dermatologists still insist upon the 'herpetic' character in a large number of instances where a gouty condition can hardly be traced. This undue extension of the connection does not, however, invalidate the facts originally pointed out.

Rendu does not believe in any distinctive peculiarities in the appearances of gouty cutaneous eruptions, as compared with other forms. Neither their polymorphous character, their circumscribed distribution, nor their occasional asymmetry are to be regarded as diagnostic. He is also sceptical as to the diagnostic value of the sensations of prickling, hyperæsthesia and hyperalgesia, upon which Bazin formerly laid stress.

Eczema.—No other disease of the skin can compare with eczema in respect of the frequency and the closeness of its association with gout. According to Garrod, no fewer than 30 per cent. of cases of inveterate gout would suffer. Eczema might almost be regarded as the cutaneous form of gout, so intimate is its relation with the disease. Not only is it capable of alternating, in hereditary transmission, with arthritic gout and with gouty neuralgia (a remarkable instance of this alternation was related to me by Dr. Bowles, in which the grandfather had severe gout, the son severe eczema, and the grandson tic douloureux); but it may at times in the individual take the place of the arthritic seizure, or precede for an interval of years the onset of the arthritic period. Indeed, in some instances the arthritic period may never be reached, and eczema then becomes in the clinical history an isolated manifestation of gout. More commonly, however, its later visitations may even be delayed, as pointed out by Garrod, till advancing age has considerably reduced the liability to the arthritic ills. It presents every degree, its severity varying with the constitutional state at the time, and being largely determined by any personal predisposition to cutaneous troubles. Its acute form, especially distressing when combined with urticaria, and its chronic dry form, are both rebellious to local measures, and sometimes difficult to cure even by constitutional remedies. The affection is, like gout itself, prone to occur in spring and autumn, but particularly in spring. Symmetry is a well-marked feature of gouty eczema, which also presents other peculiarities.

Pityriasis rubra or exfoliative dermatitis may alternate with gout. According to Sir Dyce Duckworth, a gouty bias would be present in one-fifth of the cases. This relation is not to be wondered at in connection with the similarity which the disease presents with eczema.

Psoriasis is not a distinctly gouty ailment, the tendency to thickening of the epithelium, except under constantly renewed mechanical pressure, not belonging to the affection. Garrod traces a connection rather with chronic rheumatic than with gouty arthritis. Nevertheless, since gout attacks every constitution, psoriasis will coincide with it sometimes. This association will call for due regard in connection with the treatment.

Acne, boils, and carbuncles are all occasionally seen in the gouty. The severer affection is a relatively late manifestation, to which patients are exposed by constitutional states of depression, whilst acne and boils tend to be early incidents in clinical histories which may subsequently add arthritic gout to their record.

Pruritus and prurigo, not infrequently associated with and intensifying each other, are affections often observed in the gouty state and in gouty diabetes. The acid state which favours the gouty trouble aggravates the itching, which, however, may possess a distinct local cause, as in the vulvar, anal, and preputial forms.

Urticaria is another instance of the reaction of the skin to the influences which promote the arthritic form of gout. The frequency of nettle-rash in many who are not gouty should be remembered by the side of those instances where the same mechanism, viz., some error of diet, may provoke either the arthritic or the cutaneous gouty response. This circumstance throws into strong relief the existence of the nerve factor in gout. As to the nature of the irritant, any definite statement would be premature; but it is reasonable to assume that this would be the same in gout as in the ordinary cases.

Angio-neurotic ædema is probably related to urticaria. This rare affection may occur in gout. Graves described a case under the name of fugitive gouty inflammation.

Herpes, a frequent associate of gout, may precede, accompany, or follow the attack. Sir Dyce Duckworth calls attention to the occasional recurrence of herpes at the site of previous injuries in a retrocedent form, cutting short an arthritic attack. Severe gouty neuralgia may be complicated with shingles, though the association is by some regarded as more frequently rheumatic.

Subcutaneous Nodules.—Analogous symptoms to those now commonly recognised as rheumatic have also been observed by Sir Dyce Duckworth in two female cases of chronic gout and of saturnine gout respectively.

Xerodermia is probably, in some cases, a cutaneous degeneracy induced as a result of a distant gouty inheritance.

Æstus volaticus, xanthoma, and perforating ulcer, are also mentioned by Duckworth as occasionally observed in

gouty subjects. Painful and inflamed corns have sometimes been mistaken for gouty inflammation. The view that gouty subjects are specially prone to this troublesome ailment is not established on sufficient evidence.

## THE GOUTY AFFECTIONS OF THE ORGANS OF SPECIAL SENSE.

From a practical standpoint these affections appeal exclusively to specialists. They are mentioned here in connection merely with their clinical and pathological interest.

The Eye.—The obviousness and accessibility to examination of the changes in the eye lend to their study considerable importance from the point of view of the clinical history of gout and of its diagnosis. This is specially true of the superficial changes implicating the conjunctiva and the palpebral margin. In both these situations we recognise at first sight the distinctive irritability of gouty mucous membranes. The use of the terms gouty conjunctivitis and gouty blepharitis may be considered justified by the facts observed.

Situated more deeply, but still within easy range of observation, may be recognised the changes due to *gouty episcleritis*, *sclerotitis*, and *iritis*. The symptoms of these affections are familiar. We note that they are often attributed also to rheumatism.

The remaining changes are matters for deeper investigation. They include glaucoma, hamorrhagic retinitis,\* and choroiditis.

Brudenell Carter is of opinion that much so-called gouty or rheumatic ophthalmia is glaucoma occurring in a subacute or remittent form.

<sup>\*</sup> Described by Hutchinson, 'Clin. Soc. Trans.,' vol. ix., p. 132, 1878.

The whole subject of the gouty affections of the eye has received much attention from Mr. Jonathan Hutchinson.\*

The Ear.—The occurrence of tophi in the auricle does not require any further notice. Affections of the external auditory meatus, especially eczema, are sometimes referable to gout. Garrod, who has taken notice of these lesions, and of the thickening of the tympanic membrane which may be thereby induced, has failed to trace any uratic deposits in the tympanum, or in connection with the joints between the ossicles or with their ligaments. No further information has been forthcoming on this subject.

Deafness may be sometimes due to a gouty influence, when not otherwise to be accounted for. This perhaps might explain a proportion of the instances of so-called nerve deafness; on this point no definite evidence is available. Rendu describes the onset of deafness in gout as more or less characteristic, insidious, slow, and progressive, and unaccompanied with pain or tinnitus.

Auditory vertigo is regarded as rare in gout, most instances of giddiness occurring during gouty attacks being connected with the stomach rather than with the labyrinth.

<sup>\* &#</sup>x27;A Report of the Forms of Eye Disease in Connection with Rheumatism and Gout.'- 'Ophthalmic Hospital Reports,' 1873, and various other publications.

#### CHAPTER XXVIII.

#### THE NERVOUS SYSTEM IN GOUT.

DEEPLY as the nervous system is implicated in the gouty manifestations, we are ignorant of its pathological, and know little of its clinical, aspects in connection with gout. Gouty lesions have not been found in the nervous substance, though uratic deposits have, in rare instances, been detected in the meninges and in the meningeal fluids (cf. Rendu). Dr. Buzzard believes that they may occur in the lymphatics of peripheral nerves, and set up a gouty neuritis. Sir W. Wade's\* neural theory of gout is founded upon this assumption.

Of the frequent association of a gouty history and of goutiness with the severest form of neuralgia, tic douloureux, and with a great variety of neuralgiæ, including hemicrania and sick-headache, and of minor nerve symptoms, there cannot be a doubt. Many neurotic conditions are ascribed to gouty influences, perhaps correctly; but we should not lose sight of the insecure character of this inference so long as it remains a purely clinical one.

A complete account of all the varieties of nervous ailments which have been attributed to gout cannot be attempted here. The sum of what we know is but small, and may be arranged under the headings of the anatomical divisions of the nervous system. In each category we meet with two types of ailment, the *organic* and the *neurotic*, but the line between them cannot always be firmly traced.

#### GOUTY CEREBRAL AFFECTIONS.

The Organic Cerebral Affections.—Apoplexy and cerebral degeneration, however frequent in the subjects of inveterate gout, are not in themselves gouty events. The arterial disease, their immediate cause, though it may be influenced by gout, has often a different origin. Nevertheless, the clinical events are capable of bearing a distinct relation to articular gout, through the occurrence of metastatic cerebral congestions determining a vascular rupture. The same mechanism which is observed in a sudden suppression of a gouty inflammation may also explain apoplexy, where undue strain has been thrown upon the excitable circulation of a gouty subject by mental shock, overwork, or other excitement; and this points to obvious conclusions in practice.

Gout in Hemiplegia.—It is well known that articular gout supervening upon hemiplegia usually attacks the paralyzed limb. Cases of this sort have been under the observation of every hospital physician. Sir Dyce Duckworth draws attention to the fact that the rule is not absolute; he gives an instance of the incidence of gout on the non-paralyzed limb, and another instance in which both limbs were affected.

Cerebral and Meningeal Congestion. — Extensive and severe congestions are themselves closely associated with organic results, and may be fitly considered under this category, however closely allied they are to those more limited vaso-motor disturbances which must underlie the neuroses to be presently described. The genuineness of

the occurrence of intercranial congestion on the too sudden suppression—especially by cold applications—of the acute articular symptoms is attested on sufficiently reliable authority to be accepted as a fact.

Moreover, the *symptoms* tell us of the nature of the process; they consist of violent headache, drowsiness or stupor, convulsions or vertigo. By the side of these less unusual results, extraordinary cerebral phenomena, occasionally observed in articular, but chiefly in retrocedent gout, have been attributed to similar congestions, though the evidence on which this inference is based may not be considered sufficient to exclude the alternative inference of a possible ischæmia.

Gouty Cerebral Encephalopathy.—Under this one term, which is a sufficiently neutral pathological expression to fit all varieties of these obscure and hitherto inexplicable phenomena, have been included the whole group of alarming, though, happily, relatively harmless cerebral seizures. Roughly, they may be divided into two groups:

- I. The hemiplegic form presents characters sufficiently indicated by its name. In this case the metastatic process sets up symptoms which may simulate apoplexy so closely that their complete cessation after a few days may be the only means of identifying their independence from any hæmorrhagic lesions. Rendu, who does not doubt that they are due to localized cortical congestions, quotes two of the cases reported by Lynch,\* and one by Brongniart.†
- 2. The aphasic or amnesic form is much more common and less severe. There may be slight alternation of consciousness, or even slight convulsions; but the characteristic event is the more or less marked aphasia or amnesia

<sup>\*</sup> Dublin Quarterly Journal, 1856.

<sup>† &#</sup>x27;Contribution à l'Histoire de la Goutte Viscérale'; Paris, 1875.

which, when first observed, often suggests the possible occurrence of some slight limited hæmorrhage in connection with the speech centres. The symptoms, however, will disappear completely after the lapse of a few days.

Cerebral Neuroses.—Severe ailments, such as insanity, melancholia, hypochrondriasis, and epilepsy, sometimes originate as apparent metastases of gout. The same is undoubtedly true of vertigo. Insomnia is common among gouty subjects.

We must also include here some of the minor forms belonging to the previous group. When clearly metastatic, these remarkable attacks of transient unconsciousness, of amnesia, of aphasia, or of threatened hemiplegia, have been naturally attributed to limited congestions, though, as stated above, this mode of causation is open to some doubt. On the other hand, the slighter forms are sometimes noticed independently of any acute gouty arthritis, and must then be classified as neuroses, and regarded as instances of the neurotic manifestations of goutiness.

#### GOUTY SPINAL AFFECTIONS.

The attempt is made by Rendu\* to trace to gout conditions of the spinal cord analogous to those affecting the brain. It will be seen that the clinical evidence is singularly meagre.

Gouty spinal apoplexy is represented by a single case of Critchett and Curling, who described a rapidly fatal paraplegia in a gouty subject, caused by a hæmorrhage in the upper section of the spinal cord. In this case the connection with gouty symptoms is not shown to have been immediate.

Gouty Spinal Myelitis.—Graves believed that myelitis

<sup>\*</sup> Loc. cit., p. 120 et seq.

might be induced by the extension to the cord of a gouty neuritis; he based this opinion upon the clinical and postmortem study of two cases. Here, again, the evidence hardly affords adequate support for the conclusions. Todd also reported a case of paraplegia supervening immediately after an acute attack in the feet.\*

Gouty Congestive Paraplegia .- The possibility of metastatic congestions producing in the spinal cord disturbances analogous to those of gouty encephalopathy is equally unsupported by strict evidence. Rendu adduces a case reported by Begbie, † in which an incomplete paraplegia presented temporary aggravations which were attributed to recurring local congestions of the cord. Ollivier's caset was that of a man aged forty-five, in whom gouty deposits were found in the spinal dura mater; the pia mater and the cord itself were sound. The symptoms observed were thought to have probably been adduced by gouty congestive attacks in the gray matter. Greater weight may be attached to Dr. Wilks's case, in which complete paraplegia, with bedsore and vesical symptoms, etc., set in after a gouty attack, and ultimately recovered. It was regarded as a metastasis by Dr. Wilks.§ Duckworth, + who quotes this case, believes that a paraplegia may follow or may precede a gouty attack, and may be so complete as to involve the sphincters, and yet be recovered from.

From such imperfect evidence as the above we are unable to decide in favour of the view that gout is responsible for any definite spinal affections.

<sup>\* &#</sup>x27;Cyclopedia of Anatomy and Physiology,' 1839, vol. iii., p. 121, quoted by Rendu.

<sup>† &#</sup>x27;Contributions to Practical Medicine,' 1862.

<sup>‡ &#</sup>x27;Archives de Physiologie,' 2ème série, t. v., p. 455, 1878.

<sup>§ &#</sup>x27;Diseases of the Nervous System,' 1878, p. 229.

<sup>|</sup> Cf. Duckworth, loc. cit., pp. 98, 238.

#### GOUTY MEDULLARY AFFECTIONS.

In connection with the medulla oblongata, we are restricted to the functional group of neuroses, and in particular to those of the respiratory and alimentary tracts, and of the cardiac and vaso-motor systems.

Reference has already been made to the cardio-vascular affections which have been observed in association with gout.

Among the respiratory neuroses, asthma is notoriously common among those predisposed to gout by heredity; and hay-fever is regarded by some as partaking of the same gouty bias.

Neuroses of the circulatory system are often attributed to a gouty factor. The connection in question is probably more often capable of proof in the case of the peripheral vasomotor phenomena (tingling, numbness, etc.) than in the cardiac neuroses, such as Graves' disease, tachycardia, bradycardia, and pseudo-angina. Organic angina pectoris doubtless attacks gouty subjects, but is not, any more than the atheroma to which it is due, specifically gouty.

Neuroses of the Alimentary Tract. — Esophagismus, hiccough, gastralgia, paroxysmal gastric flatulent distensions, heartburn, acute nervous dyspepsia (both gastric and duodenal), colic, and irregular action of the bowels, are some of the functional disorders, elsewhere referred to, to which gouty subjects are liable.

The stomach is the seat of the most common and of the most severe metastatic disturbances, which are in part nervous phenomena. Vertigo, as it occurs in gout, is in a majority of instances a gastric reflex, although in some cases it may be associated with other nervous symptoms suggestive of a central origin.

#### GOUTY AFFECTIONS OF PERIPHERAL NERVES.

The peripheral nervous system supplies instances of both the organic and neurotic kind.

Gouty Neuritic Varieties.—Peripheral neuritis itself had not, since Graves wrote, been definitely accredited with a gouty ætiology, until the subject was recently revived by Dr. Buzzard,\* who describes cases beginning with 'pins and needles,' and leading to muscular wasting and to changes in the electric reactions, which he was able to trace to gout, and to relieve by appropriate treatment. In connection with them, he suggests the probability of uratic deposits in the lymph channels of the nervesheaths.

The same subject is dealt with by Sir Dyce Duckworth,† who finds that, next to the great sciatic, the branches of the brachial plexus are the most commonly affected; and he refers the symptoms to an inflammation of the perineurium, with effusion into the sheath.

The inveterate neuralgia following herpes zoster, an affection regarded by various authorities as commonly of gouty origin, is probably often connected with structural changes akin to neuritis.

Under the broad heading of neuralgiæ instances of both varieties may be found. Perhaps one of the most common and most severe of those neuralgiæ which may be termed neuritic is sciatica; and gout is usually admitted as being often the cause. At the same time, it is generally held that some forms of sciatica are largely or entirely neurotic.

Again, in trifacial neuralgia, also frequently gouty, a neurotic element is undeniable. But the inveteracy and almost incurable character of the affection warrants the

<sup>\* &#</sup>x27;Paralysis from Peripheral Neuritis,' 1886.

<sup>+</sup> Loc. cit., p. 305.

view that structural changes also form part of it, and this is partly borne out by the success which the writer has found in a treatment by those remedies which promote absorption.

Gouty Neurosal Varieties. - Most of the common neuralgiæ belong to the neurosal group: the supra-orbital, the occipital, the cervico-brachial, the intercostal, and the sciatic neuralgiæ are those most frequently observed. They are easily excited in gouty subjects by comparatively trifling irritations, and not easily relieved except by appropriate treatment, or by the supervention of an articular attack.

Fugitive pains, often of considerable intensity, are apt to occur in various situations in direct association with the liability to the articular manifestations, the advent of the latter causing their immediate cessation. They probably originate from irritation of nerve-fibrils, and this is rendered the more probable by the diversity of the tissues which are their apparent seat. Sir Dyce Duckworth, who has bestowed much attention upon this subject,\* attributes them to 'a temporary local stasis of sodium urate,' and draws attention to their having been recognised as truly gouty by Anstie, t who was not a believer in a gouty causation of neuralgia. Gairdner had long ago described cases of this sort.

Gouty cramp is regarded by Rendu as induced by a local nerve irritation.

Fugitive peripheral paralysis also belongs to the neurosal category. Garrodt mentions a case of facial palsy which disappeared on the occurrence of regular gout. A similar case of temporary neuralgic paralysis of the lower limb,

<sup>\* &#</sup>x27;St. Bartholomew's Hospital Reports,' 1879, vol. xv., and loc. cit., p. 230.

<sup>† &#</sup>x27;Neuralgia and its Counterfeits,' 1871. ‡ Loc. cit., p. 548.

which was dispelled by articular gout, was observed by Graves.

Fugitive vaso-motor phenomena of ischæmic, hyperæmic, or ædematous type form a very large aggregate of minor ailments, not exclusively gouty, but often, indeed, observed in goutiness. Their detailed clinical description need not here be entered upon.

Megrim is not to be classed among the common neuralgiæ, being rather, according to Dr. Edward Liveing's happy description, a 'nerve storm.' It is not, therefore, a neuritis, but a neurosis, probably originating in the medulla, and running its course peripherally. Dr. Liveing has recognised its frequent association with a gouty tendency; and Duckworth regards it as attacking the subjects of inherited goutiness, rather than sufferers from actual gout. Dr. Haig attributes it to the presence of an excess of uric acid in the blood.

Entirely different is the simple gouty headache, which Duckworth describes as being imperfectly localized and alternating with articular attacks.

#### GOUTY AFFECTIONS OF MUSCLES.

The uratic infiltration of the tendons adjoining gouty joints may extend into the muscles. The recorded occurrence of a uratic deposit in the myocardium opens up the possibility of intramuscular deposits occurring at a distance from joints. Hitherto the clinical events have not been traced to any definite lesions.

The symptoms observed in gout are of the painful and of the spasmodic variety. Lumbago, intercostal rheumatism, and other painful myalgiæ, have often been regarded as more closely allied to gout than to rheumatism. Most probably they are due to an affection of the fibrous, rather

than of the contractile, elements of muscle. Cramp is one of the most familiar features in gout, occurring, as stated by Garrod, as a premonitory symptom of the acute attack, and also as one of the attendant symptoms of goutiness. Both in gouty cramp and in the gouty myalgia it is an open question whether the cause leading to the painful contraction or stiffness may not reside in the irritation of nerve-fibrils distributed to the fibrous tissue, rather than in any direct irritation of the muscular tissue itself. Among the spasmodic affections may perhaps be mentioned the unnatural grinding of teeth during sleep which was described by Graves, and cases of which have been recorded by other authorities.

#### CHAPTER XXIX.

### SIR WILLOUGHBY WADE'S NEURAL THEORY.

SIR WILLOUGHBY WADE'S investigations\* were suggested by a consideration of the multiplicity of the phenomena indicating the nervous system as implicated in gout, and of the absence of any precise indication that any one portion of the central nervous system is directly or indirectly identified with its production.

#### SIR W. WADE'S CLINICAL OBSERVATIONS.

The Lines of Tenderness over the Gouty Joints.—The earliest observation was that of a 'patchy' tenderness of the skin in acute gouty arthritis, without any corresponding differences in the appearance of the localized tender areas. Subsequent investigations defined these areas into narrow lines of acute tenderness. In the case of the great toe, the tender line extends beyond the zone of redness and swelling slantingly upwards to the bend of the ankle, in the area of distribution of the nerve to which Sir W. Wade refers as No. 4.†

<sup>\* &#</sup>x27;On Gout as a Peripheral Neurosis,' by Sir Willoughby Wade, M.D., F.R.C.P., Consulting Physician to the General Hospital, Birmingham. London: Simpkin, Marshall, Hamilton, Kent and Co., Limited. Birmingham: Cornish Brothers, New Street. 1893.

<sup>† &</sup>quot;No. 4 is a division of the dorsal branch of the peroneal nerve giving filaments to the foot, the inner side of the great toe, the outer

Sir W. Wade satisfied himself that this tenderness could not be referred to the tendon of the long extensor of the great toe, nor to the veins, though the latter are apt to be tender on pressure, or, at any rate, the skin over them.

Not only was there no tenderness in the intervals between the lines specified, but movement of the joint itself gave no pain, even though the bones were brought against each other with considerable pressure.

In the hands, Wade recognises four situations in which gouty attacks may occur separately or simultaneously: (1) the knuckles; (2) the back of the hands; (3) the ball of the thumb; (4) the hypothenar region.

In the hypothenar region a tender point is found on the radial side of the pisiform bone. Another tender spot is the interval between the two extensors of the thumb. A third seat of tenderness is the centre of the dorsum of the wrist, where a branch from the ulnar joins one from the radial nerve. Lastly, at the wrist-joint the ulnar nerve gives off a deep branch\* which supplies the metacarpophalangeal joints of the ring finger, of the second finger, and of the fourth finger. Wade also found tenderness in the nerves which run one on each side along the dorsum of the fingers, and one on each side on their palmar aspects. General tenderness of the fingers may, however, render the sites of these nerves difficult to distinguish.

As regards the aching and tenderness so often present in the great toe of gouty people, this can be shown to be independent of movement of the joint, and entirely connected with pressure on the inner and outer branch of the

side of the second and the inner side of the third toes."—Swan, "Demonstration of Nerves of the Human Body," Plate XXIV., Fig. 2. No. 4 nerve divides at the middle of the lower border of the anterior annular ligament into two branches—one slanting across to the base of the great toe, the other proceeding to the other toes.'

<sup>\*</sup> Swan, Plate XXII., Fig. 2, No. 28.

internal plantar nerve, and the tenderness extends also up and down their course.

The 'side tenderness' of the great toe is probably due to the internal branches of the peroneal (i.e., external popliteal nerve).

In the so-called *plantar tenderness* Wade has found a line of tenderness near the inner margin of the sole where a nerve lies to which he refers as branch 5.\*

The heel is supplied in its inner half by the posterior tibial nerve, behind the inner ankle; its outer half is supplied from behind the outer ankle by a joint branch from the communicating tibial of the sciatic, and from the cutaneous of the peroneal.†

Undue tenderness in any of these situations, even in the absence of conscious gouty feelings, points to goutiness, and may enable us to identify as gouty some otherwise unexplained visceral symptoms. It is noteworthy that, like the pains of gout, the tenderness may be fugitive.

The atiological influence of injuries is studied in different sets of cases. Different degrees are recognised:

- (a) That of severe sprains, bruises, or blows. I. The result may be immediate or long delayed. During the interval there may or may not be freedom from symptoms due to the accident itself. 2. In some cases other joints are affected also, but these have not been found affected independently of the injured one.
- (b) As instances of minor influences of the same kind are noticed: I. The determination or reproduction of joint trouble by use of the part. 2. The influence of
- \* 'Swan describes (Plate XXV., Fig. 3, No. 8) a branch of the branch 5 of the inner plantar nerve terminating in the joint of the great toe, between the metatarsal bone and the first phalanx.' This branch 5 has been already referred to as running on the inner side of the inferior aspect of the great toe.

+ Swan, Plate XXV., Fig. 2, Nos. 20 and 21.

pressure, e.g., a persistence for three days of redness and tenderness of the heel, where it had been bearing upon the opposite instep. 3. That of cold and wet feet, just as gouty inflammation may settle in a mucous membrane from cold. 4. Both neuritis and neuralgia may also be produced. 5. 'Gout in the stomach,' according to Sir Thomas Watson, 'resolves itself often under the influence of an emetic into pork in the stomach.' Taking another view, this would be an instance of visceral gout being set up by a local irritant.

#### SIR W. WADE'S THEORY.

As to the local nerve conditions, Sir W. Wade notes merely their general resemblance to those of neuralgia, hyperæmia, and neuritis of the acute and chronic form. Hyperæmia of nerves is the basis of some neuroses, whilst neuralgia and neuritis are among the recognised train of gouty symptoms.

Wade inclines to regard the conditions he has described as essentially neuritic. Of neuritis he recognises two types, implicating respectively the conducting grey matter and the protective coverings, along two lines of extension: more commonly the upward extension, as in neuritis ascendens, the influence sometimes travelling up as far as the cord itself, and sometimes the downward extension, as in neuritis descendens.

In the ætiology and in the clinical features there are strong analogies between the gouty symptoms and the classical neuritis: for instance, the more intense and early implication of the sensory nerves; the fact that the sensitiveness to pressure is constant, not, as in neuralgia, inconstant; the trophic disturbances of the skin, nails, and joints (glossy skin, etc.); and the vaso-motor disturbances.

Attention is also called to a degeneration, of toxic origin, of the white substance and of the axis cylinder. The painlessness of diphtherial neuritis is attributable to the absence of changes in the neurilemma.

In conclusion, Cullen had taught us the intimate connection between gout and the nervous system; the connecting bond, according to Wade, is in the peripheral nerves.

Returning to a consideration of the acute local gouty attack, Wade distinguishes two sets of cases. In one of them he regards the neuritis as set up by primary inflammation of the joint. In another class he finds a neuritis present, but arthritis absent. Thus, he mentions the concurrent presence in a patient of a gouty affection of the thumb without arthritis, and of a gouty affection of the fingers with arthritis and effusion.

The evidence of the priority of the nerve disorder is to be traced in the sensory, the vaso-motor, and the trophic changes. The missing link in the demonstration is the proof of a pre-existing neuritis culminating in a frank arthritic attack. This link should be sought by careful observers. One difficulty is often that of determining whether an instance of tenderness due to an inflamed nerve fibril is or is not connected with a joint inflammation. The tender nerve renders the part as a whole intolerant of the slightest movement, though the joint may not be affected.

Sir W. Wade's Theory of Gout.—Taking a view of the whole subject of gout, Wade assumes an aberration of the metabolism of proteids (a hypo-metabolism or parametabolism of unknown cause, origin, and stages). Meanwhile, quadriurate of sodium lowers the alkalinity of the blood. There may be also other by-products, terminal or collateral, besides the excess of uric acid.

The disturbance of metabolism is induced by excessive mental strain, or by the use of certain foods, or of alcohol—particularly in the form of fermented malt liquors, or of strong, highly-saccharated, hyperacid, or effervescing wines of high ætherial percentage. By this faulty blood state the stability of the nerve-trunks is impaired, and they are laid open to influences which would be inoperative on normal nerves.

These are the combined intrinsic and extrinsic influences leading up to neuralgia or neuritis. The further effects are determined by the intensity of the neuropathy, by the endowments of the nerve affected (whether sensory, vasomotor, trophic, or motor), by its territorial distribution, and by the simultaneous implication of two or more classes of nerves. The blood poison seems to possess an elective affinity for the various classes in the order stated.

The neuropathy is enhanced by any sudden increase in the blood dyscrasia, owing to (I) an aggravation of the cause which disturbs the metabolism—and it may be noted that the highest and the lower cerebral centres may conceivably influence metabolic activity; (2) a liberation into the blood of the morbid products stored up in some part or viscus; and (3) a diminution in the eliminative function of some organ or organs which should have separated these products from the blood.

The properties of a neuritis, of ascending or of descending from its primary seat, and in this way even of affecting the spinal centres, or of radiating to the periphery, belong to this neuropathy. On the other hand, the central nervous centres may originate or aggravate the general gouty condition by their influence over 'recognised seats of metabolic activity.' They may also determine local outbreaks through the agency of vaso-motor nerves.

The higher cerebral centres are also liable to suffer from the blood dyscrasia (ill-temper, melancholia, etc.).

Visceral gout may be associated with local deposition of the biurate, analogous to that in the joints. Since in the latter the deposition is neither necessary nor invariable in gout—no deposit being sometimes found in a joint which had been repeatedly affected, whilst a deposit may be found long years after the occurrence of a single attack in any given joint, and that the deposit might therefore be looked upon as an epiphenomenon—its inconstancy in visceral gout is nothing more than might be expected.

In what way an attack may be transferred from a joint to some internal part, and, again, why there should be, after an articular seizure, a total or permanent cessation from those symptoms which are supposed to depend upon impurity of blood, there is at present no evidence to show.

Arguments in Favour of the 'Neural Theory.'—Sir W. Wade has restated the neural theory, hitherto discredited by its vagueness, in a form which is definite, concrete, and tangible. Neuritis, which is advanced as the principal change, may be directly concerned in implicating the spinal centres, and in influencing the cerebral centres. On the other hand, it does not exclude the direct influence exercised by the highest cerebral centres in determining the seizures, an influence which cannot be gainsaid, though it is as yet inexplicable.

Another plea is that the theory fits better than any other with the clinical facts. For instance, the excessive liability of the great toe to acute attacks is better explained by pressure on the nerves beneath and above the joint, and by neuritis, than by the alleged influence of remoteness from the heart (this being precisely the same in the case

of the other toes), or of the incidence on this joint of the weight of the body, the latter bearing with almost equal force on the ankle.

Again, the absence of any uratic infiltration in a joint which has suffered from repeated attacks supports the view that, in an ordinary local seizure, there are two elements—an inflammation of the joint, and an inflammation of the neighbouring soft parts. One of these can possibly occur without the other; indeed, in many cases the actual existence of an arthritis is matter of inference only.

It is certainly noteworthy that the earliest and severest attacks involve the superficial structures, and that those associated with considerable deposition and destruction present a minimum of inflammation of the soft parts, whilst tophi in the ears (probably induced by the weight of the head on the pillow) occur without any predisposing inflammation.

The rapid disappearance of the inflammation from the great toe under the influence of cold affusion, of colchicum, or of other means, is not easily explained by the assumption that its cause is the mechanical irritation of the biurate. The removal of the latter within so brief a space of time is not readily conceived; but neuritis would explain the clinical result.

Visceral gout, one factor of which is 'the gouty poison in the blood,' would be in part dependent on the deterioration of the local nerves under the influence of the poison, at least of such nerves as possess a neurilemma.

#### CHAPTER XXX.

# RETROCEDENT GOUT AND WANDERING GOUT, AND THE PHENOMENA OF IDIOSYNCRASY.

#### GOUTY METASTASIS.

A VISCERAL crisis, cerebral, nervous, pulmonary, cardiac, or gastric, coinciding with the abrupt subsidence of an acute joint attack, is commonly regarded as gouty, and described as *suppressed* or as *retrocedent gout*. The two names represent two pathological views of the events. According to one of them, the gouty process itself is checked; according to the other, it persists, the gouty products being merely diverted from the joint into the less favourable channel of the viscera. Reference has been made to the clinical phenomena of the chief visceral metastases. The following remarks will deal with some of the pathological aspects of the question.

The more severe metastases occur in the course of acute gout, and it is to this variety that the terms mentioned are generally applied. Another group of cases is connected with the milder articular manifestations, or with the state of goutiness, and is known as 'wandering' or 'flying' gout. The first of these is becoming infrequent; much less so the second. The acute joint attacks are now less common, and a revulsive treatment favouring metastasis is less often resorted to than in former genera-

tions. Moreover, angina pectoris and locomotor ataxy now claim a proportion of the mysterious seizures formerly recorded as metastatic. This has caused the nature of the remaining cases, and the genuineness of gouty metastasis itself, to be called in question; and it has been suggested that, like so many other ancient views, retrocedent gout might be a traditional error.

We should not, however, too hastily dismiss gouty metastasis as a fable. The clinical facts, though many of them are old, are not uniformly unworthy of credence. Modern literature provides us with occasional instances which will compare with them; indeed, there has been an unbroken continuity in the clinical records from remote times down to the present day, and many are sufficiently circumstantial to enable us to gauge their value.

Retrocedence is rendered probable, moreover, by the undeniable genuineness of a converse process. Sudden and severe visceral crises are not only apt to replace a retrocedent arthritis: they may precede the latter, and be themselves replaced by it. In the latter case the gouty influence is not on the wane, but at its height at the time of the visceral seizure, which is cut short by the gouty climax in the joint. This is probably the strongest argument in favour of the gouty complexion of the whole group of the retrocedent and of the wandering visceral symptoms.

## THE PHENOMENA OF IDIOSYNCRASY: A PARALLEL WITH METASTATIC GOUT.

Severe and unaccountable symptoms, independent of gout, are sometimes set up by agencies absolutely harmless to normal persons, in connection with individual peculiarity or idiosyncrasy. Quite irrespective of the fact that the subjects in question often are potentially or

actually gouty, there is a close outward resemblance between the phenomena of gouty metastasis and some of those due to idiosyncrasy. Commonly the idiosyncrasy consists in a remarkable intolerance for some article of diet, which, when ingested, may cause gastro-intestinal irritation. In others there is abnormal excitability of the nervous system, and particularly of the mucous membranes of the organs of special sense—as in asthma and hay-asthma. A publication of the following instances is kindly permitted by Mr. George Pollock.\*

'The following instance was related to me by the late Dr. Roupell. A relative of his could not partake of rice without most alarming symptoms. . . . Some friends wished to test the truth of this peculiar or supposed effect of rice, and, knowing that he was fond of biscuits, had some prepared with one grain of rice in each. These biscuits were placed near him after dinner, and he partook of two or three. He became uncomfortable, and had to leave the table, observing at the same time that, if he were not morally certain that he had not partaken of rice at dinner, he was being poisoned by it.'

'Another amusing instance is that of a man who could not eat gooseberries without their producing an eczematous eruption on some part of the body. When dining with a fashionable party, soon after the champagne had been handed round, he observed to a friend sitting next him, that the wine was not champagne, but gooseberry wine, and, pulling up his shirt-sleeve, showed him the specific eczematous rash appearing.'

'Sir Russell Reynolds has sent me the following notes:

"An elderly lady and patient known to me was highly

<sup>\*</sup> Cf. 'Address delivered at the Opening of the Classes of St. George's Hospital Medical School, Session 1895-96,' by George Pollock, F.R.C.S.

susceptible to the influence of opium in any form, even to the minutest dose, its use inducing symptoms like Asiatic cholera. . . . In prescribing for her, when suffering from bronchial catarrh, I put in ten minims of compound tincture of camphor. About half an hour after I was summoned, and found that she had been vomiting and purging, and was in a state of collapse. . . . In this case the dose of opium must have been ½4th of a grain."

'A gentleman has sent me the following particulars of his own case: "A mere spoonful of honey will cause sensations of indigestion — a burning sensation in the throat, shortness of breath, and giddiness. This generally lasts for two hours after having tasted the honey. Honey has had the same effect on me ever since my childhood."

'Another gentleman writes: "I have never, at any time, been able to partake of eggs, in any shape or form of cookery, without subsequent very unpleasant results violent pain and sickness."

'A gentleman always had to avoid turpentine, as it caused his skin to swell and blister, accompanied by acute pain. One day his arm swelled suddenly, and the swelling was so great that in the end the coat-sleeve had to be cut open. For some time it could not be accounted for, as he knew he had not come in contact with turpentine in any way. In the end it was found out that the sleeve of his coat had been smeared with paint, and that his servant had cleaned it with the obnoxious liquid.'

Whilst lessening our scepticism in regard to gouty metastasis, these observations aid our study of the latter. The conditions related are almost those of a physiological experiment, and they leave no doubt as to the nature of the irritant. The following suggestions arise in connection with them:

(1) The visceral nervous system is capable of reacting

with a maximum intensity to minimal irritations. The severe dynamic disturbance excited by such imponderable agents as those which appeal to our senses of taste and of smell remind us of the violent response called forth by the slighter forms of superficial irritation of the larynx (e.g., by a bread crumb).

The alarming prostration often produced reminds us of the phenomena of collapse in retrocedent gout, and throws light on the delicacy and apparently purely nervous reflex mechanism by which they are probably conditioned.

(2) The *original irritant* may in gout be not less subtle than in some cases of idiosyncrasy, such as that in which a small quantity of rice, which had been added to beer in the bottling, led to severe symptoms.\* The latter case shows that the offending material may be a soluble one, and that the gastro-intestinal symptoms need have no reference to difficult digestion of solid material. Here, again, we are compelled to conclude that the influence was mainly exerted on the nervous system, and by such soluble or volatile material as might be extracted from a few grains of rice.

At the same time, both in instances of this kind and in that of gouty metastasis, the possibility should not be overlooked that the toxic effects may be due to some faulty glandular secretion influenced by the irritant, though the latter (uric acid, say) need not be toxic.

(3) The excitability of the cutaneous and mucous nervemechanisms under minimal irritation is also exemplified. In the case of irritation by turpentine, as also in cases of hay-fever, the associated vaso-motor action is also manifest.

<sup>\*</sup> This instance was related to the writer by Mr. Pollock, on the authority of Mr. T. W. Nunn, F.R.C.S.

#### THE NATURE AND MECHANISM OF GOUTY METASTASIS.

The problem of visceral gout and of gouty metastasis remains yet unsolved. Any adequate explanation should include the milder and less definite phenomena of wandering visceral gout, as well as the sudden and alarming visceral crises. Are the visceral accidents really the direct result of a cessation of the local inflammation, or are both the local check-and the visceral complication simultaneous results belonging to a given phase in the development of the gouty process in some constitutions? The distinction is a fine but not an overdrawn one. The patient may become at a certain period of his gout specially prone, on slight provocation, to pulmonary, to gastric, or other troubles, whilst the previous violence of his articular attacks may no longer prevail. The visceral trouble is still a gouty trouble, and a result of the general weakness produced by the chronic disease; but it is not in a true sense a retrocedence. It is a direct effect of the irritation rather than of the gout.

Between these two views it is difficult to pronounce, but the more closely we analyze the recorded cases, the more are we impressed with the close relationship between the local and the visceral manifestations. The cases belong to two groups mainly: those in which the visceral complication supervenes on the abrupt cessation of the articular lesion; and others in which the visceral trouble appears first, and by its suddenness, severity, and unexplained and intangible causation, is for a few hours a diagnostic puzzle, after which the wonder subsides into common articular gout. Instances are given in the treatises on gout by Sir A. Garrod and by Sir Dyce Duckworth. They bear strong witness to the genuineness of the gouty connection, for we are now agreed that the articular attack is preceded by a saturation of the blood with irritating substances, though opinions differ as to their toxicity.

Three theories might be proposed in explanation of the phenomena of metastasis. The influence might be that of a mechanical irritation, of a toxic principle, or of a nervous reflex.

(I) Theory of Metastasis by Mechanical Irritation.—Sir W. Roberts does not hesitate to assume a precipitation of uric acid in the visceral situations which become the seat of disturbance. The occurrence of visceral seizures as pre-arthritic prodromata undoubtedly lends support to this view, the blood being already charged with uric acid a few hours before the attack, the gouty dyscrasia at its height, and precipitation imminent. An opposite reasoning applies, however, to the other set of cases where the affected joint has already relieved the blood of a great deal of its uric acid excess.

Again, on the theory of leucocytosis, it is conceivable that through relatively sudden proliferation and destruction of leucocytes the uric acid production might be suddenly raised; whilst, conversely, influences rapidly modifying the leucocytosis (physical exertion, alteratives, strong mental impressions) might abruptly stop or lessen the acute articular symptoms; indeed, some extraordinary instances have been recorded in which a single dose of a remedy such as morphia, or the heroic plan of warding off the attack by violent exercise, proved absolutely successful.

There is, however, a wide gap between the recognition of abrupt fluctuations in the amount of uric acid available for precipitation, and a demonstration of the deposition in the viscera. Of this occurrence no definite proof has hitherto been supplied.

(2) The Theory of Metastasis by Toxic Agency.—Short of admitting a transference of the biurate from the uratic joint, or from the supersaturated blood to the viscus, and a mechanical irritation of the tissues by the acicular deposit, we might assume that toxic principles circulating in the blood might irritate various organs in the order of their excitability. Diabetic coma and uræmia are instances in point. Although the symptoms of uræmia are not strictly analogous to those now under discussion, the irregularities in the excretion of urea bear some resemblance to those affecting uric acid in gout; and in both instances the brain is apt to suffer, although in gout this is the exception, and in uræmia the rule.

Uræmia has received special attention in Professor Bouchard's recent studies on 'auto-intoxications.' Bouchard, as a result of experiments on animals, points out that urea is not poisonous, and that its intravenous injection into rabbits destroys life only when the quantity of urea solution injected amounts to the bulk of injection which proves fatal even when pure water is used. He gives reason for a conclusion that in uræmia it is not an excess of urea in the blood which produces the symptoms, but the substitution for it of those substances which should have been transformed into urea. In support of this view, he is able to demonstrate that on the advent of uræmia the normal toxic properties of healthy urine are lost; uræmic urine is no longer a toxic fluid.

In conclusion, the toxic theory is hard to prove or disprove. Besides uric acid, the non-toxic character of which has already been pointed out, various substances possibly added to the circulation from the faulty metabolism of gout, may be capable of toxic actions under special circumstances; but of all this we know nothing. The instances of idiosyncrasy show that the smallness of

the dose of the original irritant is not an argument against this explanation; though it would militate against the possibility of identifying the poison or of proving its ætiological influence.

(3) The Nervous Reflex Theory of Gouty Metastasis differs absolutely from the more materialistic theories, those of precipitation and of intoxication. No urate of sodium passes, in connection with the events of retrocedent gout, between blood or joint and viscus, but the sudden check suffered by the articular inflammation is merely re-echoed along and through the nervous system into those parts which at the time happen to be most susceptible, therein setting up functional changes.

Looking outside the domain of gout, we find that, with the exception of the embolic affections, migratory symptoms occurring at a distance from the source of irritation are most commonly localized in the viscera by nervous agency. The paroxysmal heart attacks of hurry or of diminished rate; the phenomena of Graves's disease and of pseudo-angina; the gastric crises of hysteria and those of locomotor ataxy; the convulsions of infants from indigestible food; the convulsive seizures of children at the onset of febrile disease, and expecially of the exanthemata; the functional paralyses, such as witnessed in hysteria, etc.; the hyperpnæa accompanied with tachycardia, seen in some cases of functional exhaustion of the nervous centres-these, and many more, are instances of deep and sudden nervous disturbances connected with peripheral irritation.

In gout itself the nervous theory of metastasis finds the strongest support in the obviously nervous causation of some of the articular attacks, particularly under the influence of excessive cerebral activity.

The mechanism of the alleged nervous agency in meta-

stasis is presumably vaso-motor, the immediate cause of the symptoms being the abrupt alteration induced in the visceral circulation. This would be but a modification of normal functions. The fluctuations between peripheral and visceral circulation are often manifested in everyday life. In pathology vaso-motor reflexes hold a recognised place, and to these we shall now turn our attention.

#### THE VASCULAR REACTIONS OF GOUT.

Whether, as contended by Sir Spencer Wells,\* predominant nervous activity is a distinct predisposing agent, or whether the nervous quickness which is characteristic of gout arises from the nutritional conditions which breed the disease, it is sufficiently obvious that the vaso-motor events are rapid and extensive in the cutaneous and general circulation of gouty subjects.

It is during the attack itself that the vascular reactions acquire an almost stormy development. The *initial rigor*, so often experienced, is the first foreboding of the storm; and it is noteworthy that this is a general symptom suggesting strongly the implication of the entire vascular system, as a storm modifies the whole atmosphere over a considerable surface.

In connection with the great toe, where the gout-storm so often breaks, the vascular phenomena are most striking. The greatly reddened and shiny skin and the abrupt cedema indicate intense local action. Its mechanism is still unknown, but that it is worked through the agency of the vascular system is not doubtful. The vessels of the part are turgid; fluid is poured out into the tissues as though to soak them and wash them out, and perhaps serves the purpose of floating the scavenger cells. Mean-

<sup>\*</sup> Loc. cit., p. 26.

while in other parts of the body pressure is got up by vaso-constriction, and under this stimulus the heart acts vigorously, whilst the pressure from the local vaso-dilatation is probably the cause of much of the pain. In the general cardio-vascular excitement we have the indication for a remedy such as colchicum, and a partial explanation for its beneficial action.

The Hyperæmic Processes in Visceral and in Retrocedent Gout.—Hyperæmia is probably the prevailing feature in visceral gout. In the alimentary tract the congestive form of metastasis is that with which we are most familiar. We find it in the liver, spleen, intestine, and stomach. Of all these varieties, metastatic gouty gastritis is the affection most often described and most dreaded. Three modes of origin have been assigned to it: (a) The local irritation produced on the mucous membrane by an illtimed and an ill-planned meal; (b) the local irritation attributed to a local deposition of biurate crystals, supposed to take place in its walls; (c) the influence of a central irritation of the vagus reflected to the stomach. That these provocations should lead to congestion is a reasonable inference. Evidence to that effect is, however, very incomplete. In the rare instances in which the post-mortem appearances of the stomach after metastatic gastritis have been reported, congestion of the mucous membrane has been observed.

The Ischæmic Processes in Retrocedent Gout.—Among visceral and retrocedent attacks there are probably more instances of the ischæmic process, and in the visceral manifestations of goutiness there is probably more of ischæmia, than we have been accustomed to suspect. At any rate, the tension of pulse so often observed, even anterior to any kidney disease, suggests peripheral vaso-constriction. Among the visceral seizures attributable to ischæmia, none

are more striking than some of the functional cerebral attacks with affection of speech and of memory, described under gouty encephalopathy. These are clearly to be distinguished from the apoplectiform attacks so often recorded in connection with gout. Congestion is the obvious antecedent of the hæmorrhagic seizures; but it does not supply an easy explanation for the symptoms in question. But for its temporary nature and complete recovery, the abrupt loss of function of some of the cortical centres reminds us of that traced, in embolism, to the sudden cessation of the local blood-supply. It suggests an extreme degree of local ischæmia; but a demonstration of the latter has never been given.

The metastatic pseudo-anginal seizures elsewhere described supply us with equally strong inferences. The vascular factor in the causation of the true anginal attack is not congestion, but ischæmia, and if variations in the arterial calibre take any active share in the gouty metastatic anginoid seizures, they must lie in the direction of constriction rather than of dilatation.

In conclusion, the theory of mechanical irritation by migratory deposits of sodium biurate, whilst it incurs the onus probandi, inasmuch as the assumptions which it makes are within the range of possible demonstration, remains destitute of anatomical proof. Even a discovery of uratic deposits in various organs would not in itself enable us to conclude that they had been in any way responsible for the visceral seizures. Moreover, this is to a certain extent an hypothesis ex hypothesis. So long as strict proof is wanting that gouty arthritis itself is the result and not the cause of the precipitation of sodium biurate, the 'showers of urates' suggested by Sir W. Roberts would not constitute, in spite of their captivating simplicity, any definite proof.

Assuming, then, that the visceral changes are chiefly vascular, they might conceivably be caused by direct toxic irritation, or through nerve agency from a distance. Both views are hypothetical, though not equally so: we are familiar with visceral reflex phenomena, but of the supposed toxic agent we know nothing. Lastly reflex ischæmiæ and hyperæmiæ are often within the reach of clinical observation. That these are the mechanisms most commonly at work in metastatic gout is rendered probable by the rapidity of the clinical changes observed, which could ill be explained by such slow processes as those dependent upon intracellular metabolism.

#### CHAPTER XXXI.

# ON SOME OF THE CLINICAL PECULIARITIES OF GOUT AND GOUTINESS, GOUTY INHERITANCE, AND GOUTY IDIOSYNCRASY.

UNDER this heading may be briefly considered, in addition to the individual peculiarities of gouty subjects in general, those of certain groups of subjects, and particularly of the female sex before and after the menopause. Again, in connection with gouty symptoms, attention will be called to the well-known tendency to a paroxysmal and nocturnal onset.

The Relative Immunity of the Female Sex.—Deep significance attaches to the fact that women do not suffer from gout as often or as severely as men, and that prior to the menopause their liability is very slight. Most striking is their relative immunity from articular complications. Goutiness expresses the usual extent of their ailment. To all gouty nerve manifestations, including glycosuria, and to those minor structural changes, such as nodules on the fingers, etc., which are under the influence of the nervous system, they are distinctly liable; but declared articular gout is with them the exception. This marked difference between the sexes is usually explained in connection with diet; but the influence of the menopause in heightening the gouty liability of women points to there being some other modifying factor besides their habits of life.

The adaptations of the system to the possibilities as well as to the actualities of maternal life are largely questions 'beyond our philosophy,' but their influence must be great in connection with nutrition. During the sexual period of life the ever-recurring cycle of ovarian changes implies something more than a periodical emunction, viz., a perpetual employment of energy in a formative direction. The fluctuations in this expenditure are probably reflected upon the metabolism of the nervous system and of the economy, and might exercise upon them an influence distantly analogous to that impressed upon nutrition by systematic variations in the supplies.

So long as ovarian life is active, the muscular system takes a secondary part; and, as a general rule, animal food is less desired by the young female than those of the carbo-hydrate and fatty groups. With the advent of the menopause these various factors no longer prevail, and, whilst the liability to gout remains decidedly less than in the male, the balance shows a tendency to be restored.

Idiosyncrasy is a leading characteristic in gout, and whichever form it may take, it is the expression of heightened excitability and lowered resistance in general, and especially of the nervous mechanisms. That some persons should develop gout under influences which to the majority are harmless, suggests as possible an original peculiarity or latent idiosyncrasy with gout as its result; but the idiosyncrasies bred of gout are more obvious and definite.

Idiosyncrasies, being inborn, belong to the gout which is inherited rather than to that which is acquired. We have already dwelt upon some of their forms: nervous asthma, hay-fever, and other respiratory neuroses are idiosyncrasies. Instances not less familiar are those of a disproportionate reaction upon irritation of the alimentary

tract, and of reflected visceral and cerebral disturbances. Again, in the children of gouty parents the skin often affords the earliest evidence of idiosyncrasy, urticarial rashes arising from ingesta which are food to the healthy subject, but poison to the bearer of the peculiarity. A gouty inheritance is often at the root of the extraordinary digestive disabilities met with in practice. The disinclination of some children for sweets, of others for animal food, and the intolerance of some infants for milk, belong to the same class.

The peculiarities of hereditary transmission are no less mysterious, both as regards uncertainty in its incidence and variation in its form. The singular alternations between various types of goutiness sometimes witnessed in successive generations have already been dwelt upon. In connection with this, the influence of atavism is not to be overlooked. In the words of Hutchinson:\*

'We deal more frequently with inherited tendencies than with an acquired disease. The earlier the manifestation, the more probably are they due mainly to inheritance. The inheritance of gout is almost always modified by the inheritance of peculiarities of circulation, entailing liability to chilblains, cold extremities, and the like. The inheritance of gouty symptoms combines with the inheritance of scrofula also. All gouty patients are, with the rarest exceptions, more or less rheumatic, and in hereditary descent the tendency to rheumatism and to gout becomes inextricably mixed. Such affections as sciatica, lumbago, arthritis of small joints, and crippling affections of single large joints, may be trusted to a very considerable extent as implying inheritance from gouty ancestors.'†

<sup>\*</sup> Archives of Surgery, July, 1895.

<sup>†</sup> In this connection Mr. Jonathan Hutchinson states in the Archives of Surgery for June, 1896, p. 56: 'The association between inherited

'The arthritic affections which are due to acquired gout are usually extremely painful; but those due to an inherited tendency are often insidious and almost painless.'

The peculiarities in the march of the disease are chiefly those of its periodicity and of the paroxysmal character of its manifestations.

Various explanations have been offered for the recurrence of gout at definite seasons of the year; into this question we need not enter again. There is some analogy between the seasonal periodicity and the peculiar preference shown by the more acute gouty manifestations for an occurrence during the night, and to this subject we shall devote a few concluding remarks.

#### THE NOCTURNAL EVENTS IN GOUT.

A remarkable feature in the history of gouty events is their preference for a nocturnal onset. The most common nocturnal trouble is *insomnia*, and its peculiarities are suggestive of the kind of influence which may govern the whole group. Nothing is more common than for a gouty person to be suddenly aroused, after a sound and rather heavy early sleep, by some internal discomfort, frequently connected with indigestion. In other cases the awakening remains unexplained, but sleep will not return for an hour or two, or longer.

It is almost precisely at the same time of night, viz., about two o'clock, that the gouty asthmatic will begin to suffer from his dyspnœa, the gouty bronchitic from his cough, or that palpitation or angina will seize upon the

gout and gonorrheal rheumatism is one respecting which I have long entertained no doubt whatever. Of late years I have never seen gouty rheumatism without obtaining the history of gout in the family.'

patient with a neurotic heart. Again, wandering fibromuscular pains, stiffness, cramp, neuralgia, and a host of troubles, will now make their beginning; or there may be irritability of the skin. Lastly, it is about this time that the acute arthritic attack will suddenly break upon the scene.

The uniformity in the time of onset of many of the gouty manifestations, and of those more purely neurotic, furnishes an argument for the view that gout itself is a neurosis. We cannot place much reliance upon evidence of this kind so long as the mechanism of the nocturnal neurotic seizures remains a mystery.

An important step towards the elucidation of this broader question has been made by Bouchard in his researches on the relative toxicity of the urine secreted at different periods during the twenty-four hours.\* His conclusions relate to the varying quantity and to the varying quality of the toxic matter excreted.† The urine of the night has been found experimentally to be decidedly less toxic (in the proportion of I to 2, or I to 4), although in other respects more concentrated than that of the day—a circumstance suggesting at any rate a lessened intensity of toxic elimination during the night, though not affording any evidence as to the relative intensity of toxic production; but it possesses the toxic properties of a convulsant, whereas that of the day is narcotic.

The liability to nocturnal spasmodic affections might conceivably be connected with some disturbance between

<sup>\*</sup> Bouchard, 'Lectures on Auto-intoxication in Disease,' etc.; translated by Thomas Oliver, M.A., M.D., F.R.C.P., etc. Philadelphia: F. A. Davis Co.; London: E. J. Rebman, 1894.

<sup>† &#</sup>x27;The toxic principles excreted by a man's kidney in fifty-two hours, on an average, would suffice to produce in him fatal intoxication' (loc. cit., p. 35).

the normal proportions of the two sets of poisons—for they have been shown by Bouchard to be mutual antidotes—or with a disturbed relation between the production and the excretion of the nocturnal convulsing principles.

Much light is also thrown on the question by the observation that the total toxicity of urine is diminished by muscular exercise—that is, by increased oxidation—not only during the day of the exertion, but during the ensuing night.

The onset of symptoms in the small hours of the night might be accounted for somewhat in this way. The narcotic principles due to the diurnal activity of the organism might suffice to secure sleep for two or three hours only, but prove unequal to overcoming the undue influence of the nocturnal principles, whether the latter had been produced in excess or had been imperfectly eliminated into the urine.

The explanation suggested is merely hypothetical. It has, however, the merit of suggesting for the explanation of the uniformity observed in the clinical facts the operation of some general and uniform physiological process.

In connection with the physiological functions, much may be explained by habit alone. Habit may, in this instance, assist in bringing about the early sleep, in spite of some disturbance already at work. In children, usually heavy sleepers, not only is this early rest obtained, but often enough the various spasmodic affections may be seen to occur without the spell of sleep being broken. In the adult also, physiological habit might tend to delay the trouble till after the first sleep.

Again, the time of the nocturnal events may be determined in connection with some other physiological cycles, such as that of body temperature or of digestion. Bouchard

himself admits that 'the toxicity of normal urines varies according to numerous circumstances—cerebral activity, muscular activity, sleep, diet, etc.'\*

Speculations such as these may at least serve to show that any effort to identify gout with the neuroses cannot safely be based upon the mere frequency of the nocturnal manifestations common to both. They would rather suggest the view which has considerable support in other directions, that the so-called neuroses are, like gout itself, connected with, if not dependent upon, faulty chemistry, and upon autotoxis, whether by hyperproduction or by retention.

<sup>\*</sup> Loc. cit., p. 35.

#### VII.

#### GENERAL CONCLUSIONS.

#### CHAPTER XXXII.

# CONCLUSIONS BEARING UPON THE URIC ACID AND RENAL THEORY.

The preceding pages convey some imperfect idea of the extent of the subject. Far from being explained, the problem of gout seems to have grown with each successive effort to solve it. New theories are less wanted than a weeding out of some of the older ones. We should build upon well-ascertained facts only, and be content at first to ascertain, if possible, what gout is not, leaving it for the future to show what gout is.

Gout might be made too exclusively a 'renal,' or a 'hepatic,' or a 'nervous' question. Whilst in these pages we consider these three aspects separately for the sake of clearness, we shall endeavour to prove that they are in reality inseparable.

Our available materials concerning uric acid may be summed up in a few propositions:

1. Uric acid being very readily excreted by the kidney, over-production of uric acid in the otherwise healthy system is generally manifested by an increased output in the urine. This method of estimating, by means of the amount detected in the urine, the amount produced in the system is trustworthy in most instances.

- 2. To this rule gout forms an exception. During the attack of gout, as shown by Sir A. Garrod, the amount present in the blood is increased, but the urine contains less than the average; whilst in various other morbid states, but especially in leucocythæmia and in pneumonia, the blood being charged with uric acid, the urine contains an excess of it also.
- 3. The incomplete excretion of the uric acid of the blood by the kidney is a peculiarity of gout.
- 4. Another peculiarity of gout is the deposition of part of the excess present in the blood into the joints and fibrous tissues. This does not take place in the other instances of uricacidæmia.
- 5. Gout is further characterized by an habitually low percentage of uric acid in the urine; whilst, during the intervals between the attacks, the blood may contain only a very slight or vanishing amount.
- 6. The distinctive feature of gout is not so much the over-production of uric acid, which probably never equals that observed in leucocythæmia, as its defective elimination. Since, as originally pointed out by Garrod, there may be in some cases of gout no excess in the production, the latter even remaining below the average, the fault is then entirely retention.
- 7. The cause and the mechanism of the defect are not thoroughly understood. The assumption that it is a renal defect has been based upon the fact that kidney diseases, independently of gout, lead to an excess of uric acid in the blood.\*

<sup>\*</sup> Von Jacksch, in a series of twelve cases of kidney disease, found uricacidæmia in nine, four being cases of acute, two of chronic, one of lardaceous, and two of granular atrophic nephritis. The largest amounts of uric acid were found in the cases of renal cirrhosis and incipient uræmia (Levison, *loc. cit.*, p. 55).

- 8. Some weight belongs also to the observation that poisons such as alcohol and lead, which favour the development of gout, also damage the kidney, the toxic lesions presenting singularly close resemblance with those arising as a result of gout itself.
- 9. The frequency of saturnine gout was first pointed out by Garrod in 1854, and has been confirmed by many observers. Lancereaux\* found seven cases of gout among twenty-four cases of lead intoxication. This frequency possesses significance in connection with the regularity with which lead affects the kidney.
- 10. Clinical observation and experiments in animals show that lead almost invariably affects the kidney (cf. p. 173). Garrod has further shown that uric acid can be detected in the blood of sufferers from lead, even when free from any gout; and that, moreover, the amount of uric acid excreted in the urine may be reduced by the administration of even moderate doses of the pharmacopæial preparations of lead.
- II. These facts strongly favour the view that the gouty accumulation of uric acid is due to some renal defect; but the following observations greatly reduce their force.
- 12. Complete parallelism does not invariably obtain between the liability of the kidney and that of the joints. Though the kidney always suffers, the joints are not always affected. Nay; Christison pointed out that in Scotland, where gout was almost unknown, it was not observed even among workers in lead, and that in Edinburgh saturnine gout practically did not exist. This is also the experience of Professor Philipson and of

<sup>\* &#</sup>x27;Néphrite et Arthrite saturnine' (Archives Général de Médicine, December, 1881). See also Rendu's account of this subject, giving references to Charcot, Ollivier, Potain, Bucquoy, Lancereaux, etc. (Dict. Encycl. des Sc. Médicales, 1884, art. 'Goutte,' pp. 184-187).

Dr. T. Oliver in Newcastle, where spirits are habitually consumed, in preference to beer, by the working classes. Rendu\* likewise refers to saturnine gout as being much less prevalent in France and in Germany than in England. He, however, also draws attention to the fact that French observers (1) have not always found uric acid in the blood of saturnine gout (Bucquoy and Halma), or even of gout itself; (2) nor always found in lead intoxication a diminished elimination of uric acid and of urea, but sometimes the reverse (Gubler and Albert Robin); (3) nor, lastly, did they find in every case of ordinary gout a decrease in these excretions—indeed, Bouchard and Lecorché have frequently found an increase.

Discussion is paralyzed by these contradictions between authorities, in respect of the clinical and experimental evidence as to the relative amount of the uric acid excreted.

- 13. The great clinical fact observed by Christison stands, nevertheless, above controversy. Lead, per se, does not produce gout.
- 14. Christison's observations contain another negative conclusion of still greater importance: any original kidney defect due to lead, and any saturnine uricacidæmia, are not in themselves capable of inducing gout.
- 15. It also contains a positive conclusion of great value. The gout of lead-workers is brought about by some agency which is not renal, however much renal defect may add to the result.
- 16. Clear evidence of a renal lesion preceding the arthritis, such as is obtained in some cases of saturnine gout, would lend great probability to Garrod's uric acid and renal theory. A practical difficulty arises from the fact that the kidneys in early gout are not often available

for examination. Garrod has shown, however, that one or two attacks of acute gout may suffice to determine in them visible changes. The earliest changes in the renal epithelium are not to be recognised by the naked eye, and it is conceivable that kidneys reported as healthy may have been sufficiently damaged in their most delicate and essential structure to render them unfit for perfect work. Another view, previously hinted at by Sir A. Garrod, is that the earliest renal trouble may be a purely functional one, not destroying the power of secretion, but merely limiting it to the disposal of more soluble constituents. Charcot's observations bearing on this possibility have already been quoted.\*

17. A temporary renal inadequacy might thus explain the early attacks as well as the often long interval before their return. A subsequent structural change would explain both the increased frequency of the attacks, and their occurrence on much slighter provocation, in spite of treatment, and concurrently with a reduction in the production of uric acid below the healthy average—conditions strongly contrasting with the early attacks, which need great provocation, and a large increase in the uricacidæmia.

The same views would be supported by the observation that in saturnine gout, which is admittedly associated with previously established renal lesions, the gouty attacks are from the first subacute in type, and resemble the chronic rather than the acute phase of the disease both in the multiplicity of the joints affected, and in the indolent nature of their swellings.

18. Various theories, themselves destitute of any absolute evidence, have been raised in opposition to the renal theory. One of them only need be mentioned.

The theory of over-production is patronized by Ebstein, who insists that the kidney in early gout need present no abnormality except in a limited class—that of primary renal gout with granular atrophy; but that the uric acid in the blood suffers considerable increase as a result of certain tissues having assumed in its formation a share which does not normally belong to them.

#### THE RENAL THEORY QUESTIONED.

The natural tendency, when some urinary constituent behaves in an abnormal fashion, is to connect the disease with the kidneys. Sugar escaping in diabetes was thought to be the result of a renal disease. The failure of uric acid to be excreted in a normal quantity is attributed to renal impermeability. The foundation of these inferences is not in either case a strong one. Retention of uric acid might have as little to do with the kidney as glycosuria itself.

The Nature of the Renal Block.—The great fall in the uric acid excretion, described by Garrod as characteristic of the onset of the acute attack, quickly makes way for a rise, sometimes to a higher standard than in health. What are we to think of so transitory a change? If organic, the lesion must be of the slightest kind, perhaps comparable to the changes taking place within a few hours in an abortive coryza, which are definite in themselves and in their results as affecting secretion yet largely made up of a functional neuro-vascular disturbance. Such a process as this might be superadded to a more serious and chronic lesion, or might occur in a perfectly healthy kidney.

Or shall we regard the ephemeral inhibition of the excretion as produced in some other way and independently

of the kidney? A great variety of circumstances influence the production of uric acid, as shown by Horbaczewski, and its excretion, as shown by Sir W. Roberts. The excretion of uric acid oscillates even in health with remarkable ease and rapidity on the slightest provocation. Is the more regular and significant oscillation connected with a gouty attack to be regarded as anything more than an accentuation of the every-day oscillations to which much less importance is attached?

By the side of the assumed renal imperviousness for uric acid in gout there are other possibilities. A tophus is built up by progressive depositions of biurate: the presence of crystals is an inducement for further crystallization; but the original inducement, that which led to the first deposit, was of a different kind. Was it mainly a local attraction of the tissue for uric acid? Some authorities (e.g., Ebstein) would consider that it was. Indeed, apart from gout, certain glands or organs are credited with a power to store up uric acid. Similar attractions might conceivably be exerted at times by other organs, by the system at large, or by the blood.

The conditions under which uric acid is contained in the blood of the gouty have not been accurately defined. What phases uric acid may undergo even in healthy blood we cannot pretend to know, but Sir A. Garrod has himself pointed out that it is prone to undergo change, and Salomon was able to detect uric acid in perfectly fresh blood, but not after this had stood. It is not then more difficult to imagine a temporary rise in the uric acid retaining power or modifying power of the blood and of the tissues than a transient depression of the uric acid excreting power of the kidney.

However this may be, there is another and more definite aspect of the renal question, that which is connected with the secondary kidney changes, viz., with the late results of gout rather than with its alleged kidney-derived ætiology.

#### THE ARTICULAR CHANGES.

The Deposition of the Biurate.—The vicissitudes of the uric acid accumulated in the blood, and the chemical mechanism of its precipitation, have been clearly set forth by Sir W. Roberts. We must refer the reader for a detailed account of these events to previous chapters dealing with the chemistry of gout.

The articular changes, according to the uric acid theory, present two phases: I. The stage of infiltration; 2. The stage of inflammatory reaction. This is analogous to the reaction set up by a foreign body, but in this case there is often a relatively long period of tolerance.

The extreme changes now taking place are: Nutritive alterations in the cartilage and the synovia; irritative proliferation within the cells, and ultimate destruction.

The question as to whether the deposit is primarily within the cells or within the matrix has been variously answered, and is still under discussion.

#### CHAPTER XXXIII.

# MATERIALS TOWARDS A TROPHIC THEORY.— GOUT, GOUTINESS, AND THE LIVER.

THE theory just reviewed starts from the excess of uric acid, which it accepts as a fait accompli, and proceeds to study the mechanism, and the results of its precipitation. Those to which we now turn deal mainly with gout and goutiness considered as the source of the uric acid excess. They are concerned with the origins of gout.

General Features of Gout.—Not limited to any race, but excessively prevalent in some; not localized in any climate, but distinctly rare in the low latitudes; not the exclusive outcome of any form of diet, but unmistakably influenced by some diets for good and by others for evil; rare in childhood, and uncommon in women, especially before the menopause; common in middle-aged men, and appearing earliest when inherited—gout is perhaps the most transmissible of morbid peculiarities, and among diseases it would seem to be that which least departs from the normal type of life and growth. Although most commonly inherited, gout is also frequently acquired.

The general conditions favouring its development are well known; but as the tendency of some constitutions is not towards gout, it may be doubted whether in all individuals the affection could be produced at will, even by a most perverse application to the task. Dr. Haig,

however, is of opinion that any person, by using the special means to that end, might be made to suffer from uratic arthritis. At any rate, habitual excessive indulgence in eating and drinking without compensating exercise is the recognised cause of acquired gout. This suggests that we should look to the organs of digestion for the key to its pathology.

## THE CELLULAR ACTIVITIES IN CONNECTION WITH GOUT.

The part played by individual cells is still unknown, yet it is to them ultimately that we must appeal for the desired explanation. A simple study of the material absorbed from the alimentary canal shows that it consists of undissolved particles floating in a watery solution. Were this fluid to be kept circulating through the vessels only, no nutritive purpose would be effected, however rich in nutriment the fluid might be; and the same remark applies to blood plasma. They must be absorbed and digested by living cells. Undissolved nutritious particles might float for ever unused were it not for cell agency.

The digestive function of individual cells begins with the leucocytes. If, as described by some observers, it is their duty to extend their pseudopodia between the basal cells lining the surface of the villus, and to capture passing molecules, and when fully charged with these to return towards the interior of the villus, and thence make their way into the lacteals, the stress which must be thrown upon them in cases of habitual over-feeding is obvious. This is, however, but an instance of similar difficulties experienced by all other cells, and specially by the cells of the glands engaged in the metabolism of food.

#### THE LIVER AS ONE OF THE DIGESTIVE GLANDS.

With the laity, and often with the profession in their relation with patients, 'the liver' is a generic expression loosely applied to the function of the whole alimentary system. There is great practical truth in this. In connection with digestion, the liver plays a part second only in time, not in importance, to that of the stomach and duodenum. The liver exercises a direct influence over the lower alimentary tract, and an indirect one over the stomach, pancreas, spleen, and lacteals; the various functions may thus be modified for better or for worse through its agency.

On the other hand, the liver is dependent upon all of them for its raw material, the quantity and quality of which must influence the quality of the hepatic produce. Thus we might easily be misled into taxing the liver with sins which are not its own. Many a so-called 'liver attack' is really acute gastric indigestion.

This use of the word 'liver' in an extended sense has not detracted in the past from the independent consideration claimed by the stomach; but due attention has not always been bestowed upon the spleen, the pancreas, and the intestine in their connection with gout. In rousing us to a consciousness of this neglect, Dr. Mortimer Granville has done good service. Whether pancreatico-duodenal indigestion has really any ætiological influence in gout is open to considerable doubt. That it should be set up easily, and often in those whose diet is habitually imprudent, is that which we have long known, though too often overlooked. This condition would naturally coincide at times, in luxurious eaters, with the prodromata of gout, without thereby establishing any definite ætiology.

In respect of bulk and of variety, the raw material

absorbed from the intestine can compare with that derived from the stomach and duodenum. Yet little has hitherto been said concerning it. The spleen, again, must be engaged in work of the utmost importance to the hepatic function.

From any of these sources the liver may experience disappointments, or even irritations, and much of its evil reputation in gout may have been acquired vicariously.

#### THE LIVER AS A BLOOD-ELABORATOR.

It is in relation to the composition of the blood that the importance of the liver as a factor in nutrition becomes apparent. An important part of the nutritive albuminous fluids of alkaline reaction bathing the villous tract of the small intestine, and nearly the totality of the fats, in a fine state of subdivision, are taken up directly into the lacteals, and, passing through the bodies of leucocytes and of lymphatic cells, are poured straight into the blood. With an elaboration of this portion of our supplies the liver is not immediately concerned. Any toxic impurity thus directly absorbed, or subsequently developed, can only be fractionally removed by the liver during subsequent rounds of the circulation, and would doubtless help to keep up the toxic average of the blood.

The rest of the process of absorption is carried on through the radicals of the *portal vein*; and in what does it consist? A large quantity of fluid charged with peptones, with carbo-hydrates, with ferments, with pigments, and with salts, and with soluble toxic principles, whether introduced or manufactured in the digestive tract—with all these the liver has to deal. But, meanwhile, it is receiving from the digestive glands venous blood impoverished by secreting activity, a welcome diluent for

the somewhat acrid nutritive juices in transit. From all these elements pure average blood, for which contact with oxygen at the lungs is to be the finishing touch, has to be made up again by the complex hepatic metabolism. The proportion in which effete or damaged blood-cells are broken up and disposed of is no less important a matter than the due performance of the three great metabolic functions for albumens, carbo-hydrates, and hydro-carbons, and than the separation of the nitrogenous surplus and the fixation or oxidation of poisons, whether animal or mineral.

This many-sided activity of the liver as an elaborator of common food into cell-food, as a manufacturer of ferments, as a purifier and refiner of the blood, in addition to its intestinal digestive functions proper, places it at the head of all organs subservient to nutrition. No nutritive process of any importance can proceed in which it has not some share, nor can nutrition prosper if it be overtaxed or paralyzed.

#### THE LIVER IN RELATION TO URIC ACID.

We have already dwelt upon Murchison's views as to the production of lithæmia by functional inadequacy or disturbance of the liver, considered not only as the source of bile, but as a most active centre of metabolism. Murchison did not hesitate to trace also to the liver the faulty metabolism, and by implication the excess of uric acid peculiar to gout. We can no longer subscribe to the opinion that the liver is the only agent in uricacidæmia. There is strong evidence that the production of uric acid, both in normal and pathological states, does not belong exclusively to the liver, that the spleen takes a large share in it, and that some of the uric acid may own an even wider derivation from glands and tissues.

In favour of the same conclusion, Rendu points out that many gouty subjects do not manifest hepatic complications, and that severe hepatic disease is most commonly unassociated with any gouty manifestations. It is also remarkable that in tophaceous gout, where most uric acid is deposited, the hepatic manifestations are very frequently absent. According to Rendu, uric acid, as well as urea and carbon dioxide, are formed wherever nitrogenous tissues are undergoing combustion.

#### LITHÆMIA AND GOUT.

Nevertheless, it cannot be denied that between lithæmia, as understood by Murchison, and various gouty states, a close kinship exists. Heaviness, depression, torpor, giddiness, headache, insomnia, gastro-intestinal disturbance, varicose veins, hæmorrhoids, etc., which belong to lithæmia, occur also in many cases of gout.

The lithuria of hepatic engorgement, or of lithæmia, has its analogy in the lithiasis or gravel, so familiar to us in the gouty or their descendants. The association with gout is, however, seldom immediate. Commonly gout and gravel occur in separate subjects as an alternating inheritance; or, if in the clinical history of the same individual, at wide intervals of time. We need not here point out the differences in the urology of the lithæmic lithuria and of the gouty lithiasis: the excessive pigmentation of the urine in the one, its relative pallor in the other. This difference alone would suggest caution in assimilating too closely the two pathological processes.

We should be careful not to limit the ætiology of gout, much less its pathology, to the lithæmic connection. Often enough the hepatic irregularities, which correspond in their clinical manifestations to the 'lithæmic symptoms' of Murchison, are conspicuously absent. At the same time, the various errors in diet and in hygiene, which sometimes bring about lithæmia, also lead up to gout; but here again we perceive alternation rather than identity. A patient with declared gout probably will not suffer from the usual symptoms of lithæmia, and vice verså. Yet to become the subject of lithæmia would be, for many individuals, to invite the advent of the gout. The two tendencies run on closely parallel lines, with frequent junctions.

The most that can be said is, that in some subjects, and particularly in the plethoric and torpid, the attacks of the liver are frequent and easily provoked, and that this is often evidence of a progressive goutiness.

Looking more closely into clinical histories, we may identify the tendency as inherent to certain constitutions, those naturally or by habits of life predisposed to the hepatic conditions which determine lithæmia. This brings us back to a consideration without which neither the clinical nor the pathological aspects of gout can be thoroughly understood. The constitutions which become the bearers of gout differ between themselves in wide degree, and gouty manifestations are therefore exceedingly various; but in contrast to non-gouty constitutions, those are undoubtedly more liable to acquire gout, or to develop it when predisposed by inheritance, into which enters an element of hepatic weakness or susceptibility. common impression that gout and lithæmia are convertible terms may, therefore, be traced to clinical observations in themselves correct, though perhaps not equal to so large a generalization; and it may be held that a constitutional peculiarity involving permanent hepatic inadequacy or over-strain would encourage a liability to gout.

This is not all; the relation between gout and the liver

must be viewed from the other side. Does gout affect the liver in any way? and if so, is the influence restricted to function, or does it, as in the case of the kidney, affect also the structure? We have discussed the first of these questions in the Clinical Section, and a negative answer has been given to the second under the heading of Pathological Anatomy.

#### GOUTINESS AND ACIDITY.

Excessive acidity is one of the most marked peculiarities of the gouty state, of which the patients themselves are fully aware. 'An acid stomach' is frequently the earliest foreboding of the approaching fit of the gout; but undue acidity is by no means limited to the gastric secretion: it is found in the urine and in the sweat. It also affects the blood to the extent of diminishing its alkalinity; and to this modification in the reaction of the plasma and of the juices much ætiological importance is attached in several of the theories which we have reviewed, in connection with the solubility of the urates.

Increased local acidity has been adduced by Sir W. Roberts, by Ebstein, and by others, in explanation of the intra-articular precipitation of sodium biurate. We shall not dwell upon this more limited aspect of the question, but rather upon the general acidity which is a leading factor in the production of goutiness.

Dr. Ralfe\* reminds us that the quantity of carbonic acid exhaled daily by a healthy man amounts to about 890 grammes (28 ounces), and the quantity of acid excreted by the kidney is equivalent to about 2 grammes (31 grains) of oxalic acid, in addition to an undetermined amount of

<sup>\* &#</sup>x27;A Dictionary of Medicine,' edited by Richard Quain, Bart., M.D., LL.D., F.R.S., 1894, vol. i., p. 11.

volatile fatty acids passing off with the sweat. An increase in this normal acidity would result from an undue activity of the processes which give rise to it, or from some interference with the normal process of excretion. As in the case of uric acid itself, there may be (I) an excessive production, or (2) a deficient elimination. The excessive acidity of goutiness is largely due to the latter, and its source may be traced to an imperfect elaboration of food and to an impaired metabolism of the tissues.

Digestion is obviously at fault, and the resulting abnormal fermentation of the ingesta supplies a large proportion of the acid. Often, however, the clinical history shows that the digestion was originally sound, and that the stomach has suffered with the other viscera from the long continuance of conditions affecting the general nutrition. The digestive function becomes less and less equal to the strain placed upon it by an excessive alimentation, and the acidity may persist, even after the adoption of careful restrictions.

In other cases of goutiness the gastric defect may not be prominent, yet acidity will prevail. Faulty metabolism, which is at the root of the evil in both groups, comes here more largely into play. According to Beneke, oxidation within the tissues is depressed below the normal standard, as part of a general slowing of the chemical processes of cell-nutrition. The same view is adopted by Bouchard and by Ralfe.

Thus, partly owing to an excess of nitrogenous supplies, partly owing to a slowing of tissue oxidation, the gouty acid dyscrasia goes hand-in-hand with a surplus of imperfectly oxidized residues, such as oxalic acid, uric acid, and the volatile fatty acids; and if the elimination of the latter, which in health is generally accomplished by the skin (formic, valerianic, and butyric acids), by the intes-

tine (cholalic acid), or by the kidney (uric, hippuric, oxaluric acids, etc.), should suffer a check, acute gout may ensue.

#### GOUT AS A DISEASE OF FAULTY NUTRITION.

From the various aspects under which we have considered gout we derive a uniform conclusion: The original gouty defect is not bound up with coarse organic changes. It is totally distinct from the later manifestations, and especially from the articular complications. In contrast with the latter it can hardly be identified as a disease; yet it possesses objective reality as a deviation from physiological function, and as a modification of the normal metabolism of the tissues. In a word, it is a functional derangement fraught with organic consequences, a perversion of nutrition capable of producing eventually definite structural changes.

#### CHAPTER XXXIV.

# ARGUMENTS IN SUPPORT OF THE 'NERVOUS' THEORIES.—GOUT AS A TROPHO-NEUROSIS.

Much has been made of an alleged predominance of a nervous element in gout. Cullen regarded the whole disease as primarily one of the nervous system; Sir Dyce Duckworth has advocated the view of a presiding neurosis; Charcot, Buzzard, Latham, and others, have endeavoured to explain gouty arthritis in connection with some affection of an assumed joint-centre, either medullary or spinal. All three views, with varying definiteness, claim for the nervous system control over organic processes of life. Does this power exist?

#### ON NERVE ENERGY AND ITS MISDIRECTIONS.

Of the nature of nerve energy, and of its mode of distribution, we know little, except, perhaps, that we possess some power of converging or concentrating it. We can at times definitely trace the influence of thought on function.

The oft-quoted case of Colonel Townshend, who willed himself to die, and died, is a popular illustration of the influence in question. Again, the power of the mesmerizer and the catalepsy of the mesmerized are familiar wonders; and pathology also supplies us with instances in point, whilst the cases of anorexia nervosa exemplify the degree to which nutrition may suffer under unhealthy innervation. But the greatest wonder of all is that generally referred to under the name of 'maternal impressions.' These extraordinary instances of a misdirection of energy help us to recognise the possibility of disturbances less extreme. Derangements, functional at first, and ultimately structural, perhaps arise from an imperfectly-balanced distribution of nerve force.

Our present civilization 'on wheels and on wires' tends to upset the balance in favour of nerve stimulation. Whilst saving muscular work, it draws perhaps too heavily upon our reserve of nerve energy.

The Morbid Predominance of the Nervous System.—In all processes affecting the economy as a whole, the lion's share belongs to the nervous system; and it is remarkable that, with increasing malnutrition, the steps in the hierarchy of the tissues deepen, the nervous system remaining further and further above all others. In actual starvation the nervous tissues hardly lose weight before the others have wasted.

As in starvation, or as in general malnutrition, each tissue would suffer in its own degree and in its own way, the joints in the direction of arthritis, the nervous system in the way of irritability.

The excessive nervous irritability which arises from general weakness is strikingly illustrated in the nervous manifestations, often mistermed hysterical, to which the more emotional sex is liable under temporary exhaustion. The case of the gouty is distinctly analogous. Heredity, or the long preponderance of nerve function, has brought into prominence the nervous bias, and the nervous system is ready for a special and excessive response to the operation of any general cause, such as gout.

A controlling capacity of the nervous system for the processes of nutrition might thus be admitted—at least, for the sake of argument. Let us now examine in which ways it might operate in gout.

### THE NERVOUS INFLUENCE IN THE PRODUCTION OF CONSTITUTIONAL GOUT OR GOUTINESS.

It is difficult to define the alleged influence on the general metabolism. The use of the word 'neurosis' helps thought by the analogy it suggests with familiar and tangible clinical results. If gout were a neurosis, much evidence would point to its being a neurosis of the trophic mechanisms. Unhappily, neurosis itself is a mystery.

A misdirected nerve energy might, it is alleged, set up a functional disorder leading up to structural changes. In favour of this view there is the anatomical fact that the visceral and the cerebral spinal nervous systems are in continuity, the physiological fact that these two nervous departments co-operate and mutually react upon each other, as shown experimentally by the atrophy, lower temperature, etc., of parts experimentally deprived of innervation, and, lastly, the clinical facts within every physician's knowledge. It is a matter of daily observation that the abrupt cessation of habitual muscular activity, by disturbing the balance of nerve force, will determine an attack of gout, whilst excessive muscular fatigue may have a like result. Again, extensive expenditure of nerve force from over-study, over-anxiety, grief, mental shock, depressing circumstances or illnesses, insomnia, sexual excesses, or even peripheral lesions, is a fertile source of gouty excitations. Neither should we overlook the significant frequency of an association of diabetes with gout.

On these grounds it would be hard to deny to the nervous system a leading share in the evolution of the gouty phenomena; and possibly it may play a directive part by influencing metabolism, or even the growth or destiny of cells, whether fixed or migratory. Beyond this we hesitate to proceed. The attempt to localize the primary defect in any one part of the nervous system is scarcely justified by facts. At most an argument might be derived from the facts of experimental diabetes and of diabetes insipidus, of phosphaturia, of Addison's disease, and similar neuro-trophic disorders; but analogy is not safe ground to build upon.

Contenting ourselves, then, with a broad and vague statement, we might regard gout as possibly connected with a misdirection of constructive energy under the administration of the nervous system. Abrupt deviations might be set up by accidental and temporary causes. Of this kind would be the phenomena of acute and isolated gouty attacks. Chronic deviations would result from the continued stress of more prolonged influences ultimately leading to general structural changes, in the course of which, again, the more temporary excitations would bring about the various local or visceral manifestations.

According to this interpretation of the facts, the advent both of acute and of chronic gout might be in part determined by nervous mechanisms. Meanwhile, the essential morbid process, which is to be identified by its two great features or results-undue presence of uric acid and increasing delicacy or vulnerability of structures-must be regarded as a general affection of nutrition involving all tissues; the nervous system, as in starvation and as in old age, being the last to degenerate, although its conscious or declared sufferings may be, as belongs to the most reactive of tissues, absolutely the earliest in the record.

It is just possible to think of the acute attack, per se, as some sudden and stormy disorder of the nervous system upsetting the balance of metabolism or of nutrition. It is also possible to think of the excess of uric acid as one of the results of a disturbance of the metabolism of the body, induced under the influence of the nervous system. But all this is mere speculation.

The transmission of goutiness would, according to this view, be determined by nervous agency in a manner somewhat analogous to the production of irregularities in fœtal development from mental impressions in the mother.

### THE NERVOUS INFLUENCE IN THE PRODUCTION OF GOUTY ARTHRITIS.

The Alleged Joint-centre.—A considerable step is taken in pure theory when, instead of a supposed influence on the general metabolism of the body, we are told that the liability of the joints to gouty inflammation, is directly determined through a nerve centre. This development of the theory which attributes to the nervous system a controlling power over tissues, needs proof in proportion to the definiteness of the alleged localization; and this proof is still wanting.

We have referred in another section to the arguments used by the chief supporters of a joint-centre. Rendu likewise draws attention to the determining agency of affections of the cerebro-spinal system, and to the frequency, in acute and chronic diseases of the spinal cord, of arthropathies simulating rheumatism, a connection which might explain the Protean forms of rheumatism as well as those of gout.

### THE TOXIC, MECHANICAL, NERVOUS, AND NEURITIC THEORIES OF GOUTY ARTHRITIS.

The remaining varieties of the nervous theory differ much in their explanations of the mechanism of gouty arthritis.

The Toxic Theory affords little scope for the local operation of the nervous system as a direct cause. The local acidity of the joints themselves, which has been insisted on by some authors, would be difficult to explain through a local nervous influence. On the other hand, general acidity might be satisfactorily accounted for through disturbed innervation of the metabolic glands.

It is quite conceivable that the inflammation may be due to toxic rather than to mechanical irritation. We should bear in mind that, besides uric acid, which appeals to the eye, there are all the invisible products of metabolism to be reckoned with, and above all, those acid products which seem capable, as in gouty or in simple urticaria, of determining cutaneous ædema, or, as in rheumatic arthritis, of bringing about severe and painful inflammation. The gouty acidity of the joints is sometimes adduced as an explanation for the precipitation of the crystals; might it not be the cause of the irritation and inflammation itself, as we find this to be the case in rheumatism where no solid irritant is present?

This view of gouty arthritis would not exclude uric acid deposition as an invariable concomitant. Although Rendu\* adduces Potain's observations, to the effect that a gouty person may present no appreciable trace of uric acid in the blood (whilst uricacidæmia is frequently found in conditions totally distinct from gout), we must adhere to

the view, so largely supported by evidence, that uricacidæmia is an essential part of declared gout.

The Mechanical Irritation Theory.—Here, again, we fail to see how the nervous system could prove a determining agent. Precipitation of uric acid must, as pointed out by Sir W. Roberts, be essentially a chemical process, immediately influenced by the state of the juices rather than of the tissues. On the other hand, nerve irritation may arise from the deposition; this is an inference admitted by all.

In connection with the alleged mechanical irritation by the pointed crystals, which, after all, are safely embedded in the indifferent and relatively insensitive nerveless tissues of cartilage, we are reminded of the behaviour of a variety of most sensitive tissues in which sewing needles may travel without occasioning pain or consciousness of their presence.

It has been admitted by authorities that acute arthritis has sometimes after an interval left no trace of uratic deposit in the joint affected. We should like to be assured on this point by further observations. If this were true, the view that the inflammation was necessarily due to the irritation of cartilage or fibrous tissue by sharp crystals would fall to the ground. Irrespective of any such evidence, this coarse mechanical explanation seems to be open to much doubt. Less improbable would be a mechanical irritation of nerves; but we have not hitherto recognised any crystals in the nerve substance, although the cedema and congestion are such as might result from nerve irritation.

The remaining theories appeal directly to a nervous factor.

The Nervous Theory regards the acute inflammation as determined by some nerve influence acting directly or in-

directly upon the joint. The direct form would be that suggested by the advocates of a joint centre; the indirect form is practically an instance of vaso-motor influence. Thus, Rendu regards 'articular congestion' under nerve influence as the dominant feature of the attack. He does not explain the mode of irritation, nor does he state the nature of the irritant. He reminds us that acute gout in the joints is, like acute rheumatic arthritis, often traceable to an impression of cold, and that this must operate through some nervous agency. There is, at any rate, nothing irrational in the view that the congestion and the cedema may be partly due to nerve irritation leading reflexly to local vaso-dilatation.

Sir W. Wade's Neural Theory\* seeks to explain the local gouty attack as a local neuritis. He also traces the visceral manifestations to the influence of the dyscrasia on the nervous centres. This is distinctly a neuro-humoral theory, but one allotting to uric acid a less direct share than others. The uric acid would act on the nerves first, and through their agency would influence the joints or the tissues.

As stated by Sir W. Wade, 'There is not much analogy between the special tissues of a joint and those of a mucous membrane; and into a mind dominated by the idea that, without a joint, localized gout is not possible, it is easy to see that the idea of gout in the mucous membrane will enter with difficulty.'

We will not attempt to discuss this view of the mechanism of visceral gout. In connection with gouty arthritis the neural theory has great interest. Sir W. Wade has applied to the explanation of the phenomena the latest of our discoveries in nervine pathology, that of peripheral neuritis. Instead of placing the lesion in the

<sup>\*</sup> Cf. p. 254 et seq.

central nervous system, he localizes it in the nerves of the inflamed limb.

It would be premature, before the clinical facts have been more fully tested, to reject the explanation which Sir W. Wade has put upon them. An obvious difficulty in accepting it has already been mentioned.\* It may be questioned whether the changes special to neuritis would have time to evolve and to disappear within the brief duration of some of the attacks. An acute inflammation of the lymphatics of the nerve-sheath, or an acute congestion of the vasa nervorum, would be, in this respect, more consistent with the possibilities of the case.

#### GOUT AS A TROPHO-NEUROSIS.

We may assume, with Rendu, that, while the original fault lies with nutrition and with digestion, the nervous system has an undoubted influence on the metabolic exchanges and on assimilation, and that it also exercises a determining influence upon some of the acute phenomena of gout. We must own, however, that the subtle mechanism of these influences is still unexplained. It is no less mysterious than the mechanism by which the occurrence of a severe articular attack often frees the patient from his previous ill-health.†

<sup>\*</sup> Cf. p. 258.

<sup>†</sup> Garrod explains the gouty trouble as due to an excess of uric acid, which is removed from the circulation by precipitation into the joints, and he supposes that the uric acid itself is destroyed by the agency of inflammation; but Rendu points out that, whilst it is argued that the deposit of urate sets up arthritis, and the arthritis destroys the uric acid, in tophaceous gout there is neither much inflammation, on the one hand, nor at first any destruction, but a growing accumulation of the deposit. Moreover, he points out that Garrod (cf. loc. cit., p. 386) has observed deposits in the joints of patients who had never complained of gouty symptoms.

'Neurosis' or 'tropho-neurosis' may be used as a name for this ill-defined agency, but there is no adequate proof that the nervous system is independently and primarily responsible for the production of gout. On the contrary, we hold that, in common with the mucous and cutaneous surfaces, and with the internal structures, it bears its share of the original alterations in the nutritive process. Its morbid excitability may intensify the changes progressing in other tissues, but in this there is nothing for which a parallel might not be found in other diseases not reckoned as primarily nervous.

#### CHAPTER XXXV.

#### CONCLUDING PROPOSITIONS.

ARETÆUS OF CAPPADOCIA has told us that 'of the nature of gout none but the gods have a true understanding.' This thought may allay some of the disappointment to which our present labours are doomed. We have not strictly defined gout. Nevertheless, important approaches will have been secured if the foregoing analysis of the subject should have succeeded in establishing the following points.

- 1. The assumption of the unknown factor 'diathesis' is unnecessary; and we regard the word as also superfluous.
- 2. Objectively, we deal with two states—gout and goutiness; and these names fairly express the relations and the differences existing between them. One state may never pass into the other. More commonly goutiness inclines almost fatally towards declared gout; and, with few exceptions, those once attacked with declared gout lapse, sooner or later, into goutiness.
- 3. 'Articular or Declared Gout' is the tangible result of a constitutional change, which, in the acquired form, is not at first obvious.
- 4. 'Goutiness' is applicable to all the conditions in which the *constitutional change is manifest*, though declared gout may be altogether absent, or present only at long intervals.

The evidence of goutiness may be partly structural, as in the delicacy of the tissues of those who inherit the affection; but in all cases it is also functional, and is made up of the gouty visceral manifestations.

- 5. Gout and goutiness, which diverge in their symptoms, are merged into one at their origin. Their ætiology is identical, and their treatment, so far as it is based upon their ætiology, is the same. We have no choice but to regard that which they possess in common as the essential part in them, and that which they separately exhibit as the less essential and secondary part.
- 6. Marked *uricacidamia* and demonstrable *deposits of biurates* are the features of declared gout. They are not prominent features, and may be even sometimes absent in goutiness.
- 7. Conversely, the train of visceral irregularities and disorders characteristic of goutiness form no integral part of declared gout. On the contrary, their appearance is almost evidence that arthritic gout is in abeyance; and an occasional conjunction of the two sets of symptoms is an exception which confirms the rule.
- 8. Our inability to dissever the, practically speaking, identical constitutional conditions of goutiness and of gout carries with it the conclusion that their diverging manifestations cannot be regarded as synonymous with the essence of the affection. They are merely results derived from the latter. This conclusion would dispose of the view that gout (in the more comprehensive acceptation of the term) is nothing more than a *uric acid dyscrasia*.\* It

<sup>\*</sup> Were excess of uric acid, whether due or not to leucocytosis, alone responsible, gout would be one of the characteristics of leucocythæmia; we should find it very frequently among children, whose uric acid production is great; it should be a never-failing result of certain habits of life and diet leading to daily and excessive poliferation of leucocytes.

further implies the necessity of dissociating the consideration of the phenomena of goutiness from that of the phenomena of arthritic gout, which are closely connected with an excess and a faulty disposal of uric acid.

- 9. Turning first to declared articular gout, we do not find absolute evidence as to the nature of its connection, undeniably a close one, with the deposition of biurates. Different opinions are still entertained as to whether the original deposition is the cause, the accompaniment, or the result, of the local affection; and between them we have no means of deciding.
- 10. There is no doubt whatever that the late articular changes are the direct result of the local accumulation of sodium biurate. Our knowledge of the mechanism of these changes is the most advanced department in the pathology of gout, and its early elucidation has largely contributed to a perhaps premature acceptance of the uric acid theory of gout.
- 11. Goutiness presents us with a widely different picture, the main feature of which is a general change both functional and structural, the localizations of which are accidentally determined by individual peculiarities of the subject, and the circumstances of his environment.
- 12. The functional change, as it affects the juices, is abnormal acidity; as it affects the tissues, increased irritability and lowered resistance.
- 13. The structural change is minute in proportion to its wide extent, and it probably could not be detected by the microscope in individual cells. It is nevertheless obvious; most marked is the modification of the external epithelium, and particularly that of the nails, which show decided

None of these results are invariably observed. It would be, therefore, idle to lay exclusive stress upon excess of uric acid or the agency of leucocytosis in the production of gout.

thinning. The same structural delicacy may be inferred to exist in the nervous system from a consideration of its functional relations to the skin, and of the marked increase in its excitability, and in all the tissues on the grounds of their increased vulnerability.

- 14. The question arises whether this degeneracy is merely the work of a long continuance of the acid dyscrasia, or whether it is connected with some deeperseated cause residing in the cells themselves. The former supposition is discouraged by the remarkable circumstance that the structural delicacy is transmitted to the offspring, and, indeed, is commonly noticed in the offspring of those who have acquired gout, although it may not have been perceptible in the parent.
- 15. Looking back into the clinical history of the subjects who acquire gout through high living, we often fail to trace any previous tendency to acidity. They are usually endowed with an originally strong digestion, which only gives way at the approach of the gouty stage. Moreover, extreme acidity is presented by many subjects who do not develop the slightest tendency to gout. The mode of origin of acquired gout in itself suggests the operation of some nutritional disorder, whilst the result of this nutritional defect is obvious in the eventual relative atrophy of the tissue elements.
- 16. It is conceivable that, as suggested by Beneke, the undue acidity may be itself the by-product of the faulty metamorphosis of cells. This would explain its persistence in inherited goutiness, even when metabolism is no longer oppressed and depressed by a reckless excess of ingesta. According to this view, a depressed and faulty metabolism would be the first departure, and abnormal secretion would be its outcome.
  - 17. Assuming the correctness of Beneke's view, we find

in the phenomena of goutiness a much nearer approach to some primary or essential factor than in articular gout. In the functional disturbances of the various organs we are brought distinctly nearer those intimate changes in nutrition whereby the power of resistance of tissues is lowered.

Indeed, goutiness is in varying degrees the basis of all articular gout, but most manifestly of that which is inherited.

18. The derivation of an excess of uric acid from the tissues, as suggested by Horbaczewski's researches, is consonant with the view that gout is essentially a condition of perverted nutrition. At any rate, it is highly probable that the increased uric acid production, which is undoubtedly caused by an excessive nitrogenous diet, is not largely derived from the nitrogenous foods in transitu, but is the result of an altered catabolism of the cell-substance, which is imperfectly carried out by reason of the paralyzing, and in that sense toxic, effect of the nitrogenous excess.

19. The persistence of the faulty metabolism when the original cause is no longer at work is difficult to explain. The difficulty has given rise to the notion of a 'gouty diathesis.' We prefer to deal with more tangible explanations, whilst allowing a large margin for the operation of individual peculiarity which leads in so many diseases, as well as in gout, to the immunity of some and to the liability of others when placed under apparently identical conditions. The force of habit is traceable in cellular activities, as well as in the higher mechanisms of action; it has been used as the mainspring of the theory of evolution, and may with equal probability be applied to the problem of the inheritance of gout. To say that the 'gouty diathesis' resides in the nervous system 'because

the latter governs all other tissues' is merely to shift the chief operation of this force of habit from the rank and file to the headquarters of the organism. There is much in favour of the view that the habit of faulty cellular metabolism is largely kept up by the habit of faulty innervation; but this in noways affects the proposition that all cells, including the nerve-cells, are in their various capabilities under the lasting influence of the original deviation from healthy metabolism induced by a prolonged course of toxic alimentation.

- 20. The explanation suggested has its practical bearing. Instead of a diathesis which needs 'eradicating,' we conceive of a faulty habit slowly acquired which needs replacing by a healthy habit, the growth of which must also be slow. This consideration must guide our treatment; it also encourages a belief in the curability of goutiness, though not of the late results of articular gout.
- 21. A general change, such as hinted at, must affect each element in the line of its special activity. Among organs there are those whose function is metabolism. That their deviation from healthy function should take effect out of comparison with that taken by other organs is self-evident. To this group belong the stomach, small intestine and lacteals, the pancreas and spleen, and, above all, the liver. Without attributing, with Murchison, the whole blame to the liver, we attach to its shortcomings a considerable share of responsibility; and in this we rely less on experimental evidence, for it does not furnish us with any conclusions, than on clinical observation of the events, and of the action of remedies.
- 22. Plethora has long been recognised as favouring the development of gout. Scudamore and Gairdner have, indeed, regarded blood plethora as its primary agent. Undue vascular fulness, but particularly that of the

portal system, may, as alleged, have a retarding influence on metabolism; but it might also be suggested that the normal organic activities should be sufficient to clear away the superfluous fluid. Indeed, on this point, the success of a corrective treatment leaves us in little doubt.

- 23. Gout is largely a renal question. The compensating relation so clearly shown during the attack between the joints and the kidney in connection with the disposal of uric acid is significant. Whilst the kidney refuses passage to it, the joints receive it; but this relation is quickly reversed, the renal function of the latter being restored, so far as we can judge, completely, even within the duration of a paroxysm. The subject of renal impermeability has been sufficiently discussed.
- 24. Again, much of the *prognosis* of gout gravitates round the state of the kidney. Its modern pathology might be compared to a vicious circle, of which the kidney is the centre. 'Renal defect originates the uric acid trouble, which, once started, may end in destroying the kidney.'
- 25. We are not warranted in regarding the kidney as the organ originally affected, since in some of the most stormy gouty attacks minimal changes only exist in the kidney, often so slight as not to produce albuminuria.

A strong reason for regarding the gouty trouble as one sui generis is that severe disease of the kidney need not per se lock in the uric acid or produce gout.

Were renal disease in itself capable of bringing about the uric acid disturbance and gout, all cases of lead intoxication should develop gout sooner or later; this is far from being the case. Again, all sufferers from granular kidney ought to present evidence of accumulation of uric acid, and in other forms of chronic nephritis there ought to be at least some indication of the uric acid excretion being interfered with. From the relatively small proportion of cases of gout occurring among these various groups, we conclude that some other factor besides renal inadequacy is necessary to determine the result.

- 26. Modern research indicates that, as suggested by Parkes and others, there are two main aspects to gout—the degenerative changes in the tissues, and the uric acid trouble—and that these may be simply the two phases of a single process connected with cell malnutrition.
- 27. In advanced gouty cachexia the co-existence of a prevailing systemic change by the side of the local affection is obvious. We have strong reason to believe that at earlier stages also the entire man is gouty, not the suffering joint only. In inherited goutiness structural change is likewise often manifest prior to any articular attacks. In acquired gout the constitutional change sometimes precedes the stage of acute articular attacks; it usually becomes established only after their frequent repetition.
- 28. The frequent absence of a well-marked pre-arthritic stage of goutiness in first acute attacks is partly explained in connection with the *fine balance* preserved by an essentially precarious health in all gouty states. The facility with which the balance is overthrown suggests that latent changes may have taken place unsuspected.
- 29. This *characteristic instability*, due to increased irritability and diminished resistance in the tissues, may explain the recurrences witnessed under subtle influences, such as changes of season, etc.
- 30. Gout would seem to be a typical instance of the ultimate evolution of structural changes from an affection at first almost entirely functional, and therefore capable of being controlled.

Coarse structural changes are connected with the faulty disposal of the uric acid. They constitute a totally distinct and secondary process, which should be separately considered.

Structural changes of a much finer kind, affecting the entire organism, are those resulting from a faulty metabolism. Only after a long-continued operation of their causes do they become manifest. Their full development is witnessed in the gouty cachexia of the late stages.\*

We thus distinguish, by the side of that deep-seated functional defect or error which determines gout, two progressive structural changes—the one directly affecting cell-growth in general; the other secondary, and limited to those tissues and organs in which the biurate is deposited.

- 31. The fact that gout may be acquired (all gout traced sufficiently far back must have been acquired gout) points to its functional derivation. The fact that it may, together with certain visible peculiarities recognised as gouty, be inherited, shows that its later development involves structural changes in the subject who has acquired it. These are the characteristics of a disease of faulty nutrition. The history of acquired gout is one of functional disorder leading up to organic lesions, whilst the history of inherited gout is often that of textural delicacy, leading to functional disorders.
- 32. The joints are delicate reagents for certain toxic substances, less, perhaps, owing to any high degree of sensitiveness, than owing to the slowness of the circulation of fluids through their substance, and to the peculiarity of

<sup>\*</sup> In inherited gout some part, at least, of the fine structural changes is handed down, and the uric acid troubles are called forth on comparatively trifling provocation. But since some structural gouty peculiarities are transmissible, and may be inherited even by those whose uric acid function is not perceptibly modified, we infer that uric acid troubles are not the primary cause of the gouty habit.

their lymphatics. It is still a question whether acute gouty arthritis is due to mechanical irritation by the crystals, or to chemical irritation by the concentrated solution of the sodium biurate.\* Neither the latter nor uric acid itself is toxic.

Great mechanical irritation such as would set up inflammation is not a necessary feature of the uratic deposition. Perhaps the distinction between the acutely severe and the painless form is in a great measure a question of the rate at which it takes place.

33. The extent of the arthritis associated with the periarticular swelling is matter of doubt. Sir W. Wade's observations go far towards proving that there is much less arthritis than had hitherto been supposed—at any rate, that the pain and tenderness have not their seat inside, but outside the joint, and apparently in the nerves themselves.

The facts observed by Sir W. Wade, and confirmed by others and by the writer, possess great theoretical importance.

- 34. The nervous system is largely concerned in all the phases of gout and of goutiness; and probably it also influences their mysterious hereditary transmission.
- 35. In acute gouty arthritis the share of the nervous system is variously allotted by different authorities.
- (a) Some assume a direct, others a reflected nervous action, modifying in some unexplained way the intra-articular events.
- (b) Sir W. Wade has originated the view that the *local* gouty attack is an acute neuritis, due to the local action of the biurate upon the nerves.
- (c) The writer puts a different interpretation upon Sir W. Wade's observed facts, and would regard the periarticular nerve complication as congestive, and (together

with the accompanying œdema) as reflected from the irritation by the biurate of the intra-articular nerve-endings.

36. Again, the induction of an articular seizure by nervous excitement or exhaustion is matter of every-day observation. This is another instance of the instability of the organic reactions, which is peculiar to the gouty state. If the larger share in the gouty process which we have claimed for the organs of metabolism, and particularly for the liver, really belongs to them, the nervous mechanism of the articular paroxysm might be explained. The local uratic precipitation might be the result of an acute modification in the metabolism of these organs, which are known to respond with remarkable readiness to the higher nervous centres, with which they are in direct sympathy.

The visceral manifestations of goutiness would bear an almost identical explanation.

- 37. The phenomena of retrocedent gout are probably to be regarded as the converse of this nervous process, the reflex action beginning at the periphery, and affecting the nerve-centres themselves, as in gouty encephalopathy, or being reflected from them to other viscera.
- 38. The participation of the nervous system in the slower changes which constitute goutiness and lead up to declared gout is also undeniable; but very different estimates have been placed upon it. The discussion of this intricate problem cannot be renewed here. The view which has been advocated in these pages is that the nervous system influences the faulty metabolism in the degree in which it suffers itself from the effects of a perverted nutrition. In this limited sense gout might be termed a tropho-neurosis; but it is not here implied that the process originates from the nervous system as from some independent source, external to the constitutional disturbance: the nervous system merely has a share in propagating the latter.

#### VIII.

## THE TREATMENT OF GOUT AND OF GOUTINESS.

#### CHAPTER XXXVI.

#### INTRODUCTORY REMARKS.

Various reasons invite at the present time a reconsideration of our therapeutics. In the type and in the incidence of gout definite modifications have taken place, apparently correlated with the altered conditions of modern life, which tend to modify constitutions. Recent advances in pathology have also called in question previously undoubted principles of treatment. Some radical innovations have been suggested. And lastly, the rapid progress of pharmacology has supplied us with many new remedies, the claims of which need to be considered. Before entering upon this section of our work, a few general remarks are called for.

#### EMPIRICISM AND PATHOLOGY.

A systematic analysis of the varied morbid states which have been included, sometimes without sufficient distinction, under the term 'gout' was a necessary preliminary to the practical objects contemplated in this work. Between the pathological and clinical aspect of disease and its therapeutical aspect there is a close relation. In gout, where much remains to be elucidated, the uncertainties of pathology are reflected in therapeutics, and fresh theories of treatment are the unavoidable outcome of each new pathological departure.

Long before the dawn of pathology *empiricism* was at work. Human life has ever been too short to allow the patient to wait, or the physician to strive, for a perfection of knowledge before dealing with disease. Indeed, for the greater part of his life, the physician is an empiric *ex officio*.

Pure empiricism in therapeutics is the soil in which the earliest germs of pathology are sown and developed.

Pathological theories are the upshot, and these in turn influence practice. Treatment originally empirical is now guided by theory. Nowhere is this mutual relation more marked than in the history of gout, the therapeutics of which have passed through the most varied and arbitrary phases of empiricism, and through the stage of subservience to theory, of which we are now witnessing the end.

In their modern developments therapeutics and pathology are more closely associated than ever. Their relation is one of collaboration; and it would be difficult to say which contributes the larger share.

Pathological facts should be the sole guides to treatment. This is the ideal which we have too long failed to realize, but towards the attainment of which progress is being made.

Meanwhile, in some directions therapeutics have advanced to the stage of clinical certainty; and the definiteness in the therapeutic results has become a fulcrum for pathological research, and a standard by which the correctness of some of our theoretical views may be tested. The help thus derived from a study of the treatment of gout is undoubted. The secret of the maze may often be solved by the remedy. When it succeeds, it travels through the intricate route along which we cannot follow, and by watching its operations we obtain some clue as to the points which it visits, and as to the mechanisms which it may set in motion.

The preceding remarks apply to all forms of disease. In the case of gout a special difficulty had to be dealt with: the pathological confusion resulting from an imperfect nomenclature threatened to complicate the study of its therapeutics. Indeed, the confusion which even now prevails is answerable for much of the perplexing divergence between current methods of practice. A discrimination between such essentially different conditions as those of gout and goutiness would best explain how an equal success should have been reported from the employment of opposite measures. The conditions alleged to be identical have much less in common than the misleading identity in their names would suggest. They cannot fairly be considered under the same heading, and in the following pages they will be dealt with separately.

Our inquiry into the nature of gout may have failed in its immediate object, but it will not have been barren if it has warned us against blindly trusting in any theory as a guide to treatment. Meanwhile, clinical analysis has made it clear that both in gout and in goutiness there are numerous varieties, and that, indeed, no two cases are absolutely alike. Two practical principles are its direct outcome: 'Each patient has an individual gout of his own, for which an individual treatment has to be devised;' and, above all, 'We should treat the patient rather than the disease.'

## IS GOUT CURABLE, AND SHOULD IT BE TREATED? A REVIEW OF ANCIENT AND OF MODERN SCEPTICISM.

Scepticism in Antiquity.—Each age has its sceptics in therapeutics as well as its enthusiasts. Lucian's satirical poem,  $T\rho a\gamma o\pi o\delta \acute{a}\gamma \rho a$ , part of which is here given in Sydenham's Latin translation, teaches us the form taken by the scepticism of those days, and its cause.

#### LUCIANI IRRISIO IN MEDENTES PODAGRÆ.

Quis invictam me dominam dolorum Ignorat Podagram in terra mortalium? Quam neque thuris vapor placat, Neque effusus sanguis aras ad incensas, Non templum divitiarum undique suspensis ornatum donariis. Quam neque Apollo medicamentis expugnare valet, Omnium medicus in cœlo deorum, Non filius Apollinis doctissimus Æsculapius. Postquam enim enatum est primum hominibus genus, Conantur omnes meam elidere potentiam, Miscentes semper medicamentorum artificia. Alius aliam in me experitur artem: Terunt plantagines, et apia mihi, Et folia lactucarum, et silvestrem portulacam, Alii marrubium, alii potamogeitonem, Alii urticas terunt, alii symphytum, Alii lentes afferunt ex palustribus lectas, Alii pastinacam coctam, alii folia Persicorum, Hyoscyamum, papaver, cepas agrestes, mali Punici cortices, Psyllium, thus, radicem ellebori, nitrum, Fænum Græcum cum vino, gyrinem, collamphacum, Cyperissinam gallam, pollinem hordeaceum, Brassicæ decoctæ folia, gypsum ex garo, Stercora montanæ capræ, humanum oletum, Farinas fabarum, florem Asii lapidis ; Coquunt rubetas, mures-araneos, lacertas, feles, Ranas, hyænas, tragelaphos, vulpeculas.

Quale metallum non exploratum est mortalibus?

Quis non succus? qualis non arborum lachryma?

Animalium quorumvis ossa, nervi, pelles,

Adeps, sanguis, medulla, [urina,\*] stercus, lac.

Bibunt alii numero quaterno pharmacum,

Alii octono, sed septeno plures.

Alius vero bibens hieram purgatur,

Alius incantamentis impostorum deluditur,

Judæus alium stultum excantat nactus;

Alius vero remedium petit ab hirundinis nido,

Ego autem his omnibus plorare impero.

Et facientibus hæc, atque irritantibus me,

Soleo occurrere multo iracundior;

Iis vero qui cogitant nihil adversum mihi

Benignam adhibeo mentem, facilisque fio.

Lenem, O ubique gentium celebrata, afferas nobis dolorem, O Podagra,

Levem, facilem, non acutum, brevem, haud sævientem, Tolerabilem, facile desinentem, parum validum, ambulationes non impedientem.

Multi sunt modi miserorum,
Sed exercitia dolorum et consuetudo
Podagricos soletur.
Ideoque æquo animo, O complices,
Obliviscimini dolorum:

Si ea quæ placet non fiunt,

Tamen etiam præter spem accidentibus viam invenire solet Deus.

Quivis sustineat Podagra laborantium Deludi et derideri ; Talis enim hujus morbi natura est.

This was essentially a therapeutical scepticism. Absurd and useless remedies were used, and the scepticism expressed was merely a keen sense of their uselessness. On the one hand a countless supply of useless nostrums

<sup>\*</sup> urina om. Syd.

praised up by enthusiastic empirics; on the other, the cynically expressed hopelessness of the sufferer. All this is told us in the scathing satire. Scepticism, then thoroughly justified, has survived into modern times, and, to a modified extent, still lingers among us without the same excuse. The question which it has raised must be considered.

Modern scepticism, whilst doubting the efficacy of remedies, has cast doubt also upon the curability of the disease—nay, even upon the desirability of its being treated. Gout is perhaps the only affection concerning which it has seriously been asked whether a cure was to be attempted or desired; and this question suggests that more harm than good may sometimes have resulted from the attempt. Such, at least, was the opinion of Sydenham, who did not hesitate to advocate abstention.

The well-being and comfort following a severe storm of gout convey a suggestion that the attack is beneficial. In some form or another we can trace this idea through history, and it is indicated at the close of the passage quoted from Lucian. Sydenham lent to it the support of his great authority; he regarded the fit as a happy event, a clearing of the blood which it might be dangerous, or at any rate inadvisable, in any way to check. Among the public a similar view seems to have largely prevailed.

So widespread an impression can hardly have arisen without some foundation. We are far from subscribing to the theory or to the practice in question, but we note in passing the pathological significance of any partial relief or temporary immunity possibly conferred. If the articular attack is in any sense curative, how great must be the difference between it and the morbid condition which it remedies, and which we must assume to be the constitutional state of goutiness!

As regards the curability of gout, Sydenham's somewhat gloomy conclusions, derived from personal experience, have perhaps more than any other circumstance encouraged scepticism. His doctrine of non-interference, compressed by Cullen into a well-known utterance praising the virtues of 'patience and flannel,' tended, moreover, to render a fair trial of any treatment almost impossible.

Little wonder that for a time gout suffered neglect at the hands of the profession. The undisguised independence of the unrelieved patient found a counterpart in the apathy of the physician once convinced of failure. Scudamore tells us of a distinguished physician who declined to continue his attendance on a patient suffering from an acute attack, declaring that he could do nothing for the gout.

In this way is readily explained the popularity which has been enjoyed by various quack remedies; for, as Sir Dyce Duckworth remarks, 'the appeal to quack remedies is a measure of our failure.'

The present attitude is one of compromise. Absolute scepticism in therapeutics is a thing of the past. Though we have ceased to be credulous as to the alleged virtues of most drugs, the claims of others are based on demonstration.

Among modern authorities we find no professed sceptics. Garrod distinctly holds that 'gout in its acute form is as controllable as any other inflammatory affection,' and that chronic gout may be relieved—at least, to the extent of enabling the patient to enjoy life. And others have concurred in the same opinions. Sir W. Roberts, however, whilst providing us with definite ideas as to the chemistry of gout, has expressed doubt as to the value of some of the remedies now in use. Still, he is far from endorsing in

principle the masterly inactivity of Cullen, or even the relative inactivity of Sydenham.

Our own answer to the question under consideration is: 'Gout is curable, but some of its worst results are not.' If our ætiology is right, if gout is self-inflicted, if it is the outcome of absolute or relative inactivity, coupled with over-indulgence—in short, a manufactured product of civilization—it is certainly preventable; it may even be cured after its onset. Prior to its earliest warnings, and for some time afterwards, the remedy is in our own hands. An active and frugal life is a safe preventive, and may often be a cure.

## THE PATIENT'S VIEW OF GOUT AND OF ITS TREATMENT.

Few popular fallacies have been longer cherished than the notion that gout was a harmless, nay, a beneficial affection, to be envied whilst condoled with in others, and, as Heberden pithily puts it, 'to be rather courted than dreaded by patients until they had experienced its torments.' Walpole is stated to have faced even the acute pain of gout in a spirit of thankfulness, regarding it as a remedy rather than a disease. But the time is past when the fashionable malady was welcomed with pride in spite of its dangers. The evils of gout are obvious and great, its privileges purely sentimental, and now less than ever appreciated. We hear less of the social dignity of gout; we sympathize less, perhaps, with its mode of production; we are less reckless in inviting its risks, which have now been put to the financial test. No life insurance officer fails to scrutinize the life and the family history of applicants from this point of view. In truth, in no other disease are higher stakes laid by those who court it, for the lives sacrificed to gout are usually those best worth preserving. Gout, in a word, is a much less welcome visitor than it has been; and the diagnosis of gout, when it has to be made, is more often received with disappointment, or even resented.

Treatment may always be viewed from two sides—that of the physician, and that of the patient. Of all our internal diseases, there is probably not one in which the patient, whilst racked with bodily pain, keeps a clearer mental faculty, and exercises a keener criticism; and the treatment of gout has thus been among the most freely debated in the whole range of medicine. The sufferers, themselves largely responsible for the origin of their complaint, readily take an active part also in its management, thereby sometimes checking the best endeavours for their relief. In this connection Heberden wisely remarks: 'The gout should not be considered as a reproach to medical practitioners till they are permitted to attempt a cure of the disease, or until they can find gouty patients who will follow their advice.'

Among the gouty are many distinguished by the gifts of the mind, by mental activity, and by habits of close study. Critics such as these were not likely to overlook any contradictions in medical theory and practice. Their scepticism was fully justified so long as no serious remedies were employed for their relief. Sometimes, however, when at a later date efficacious measures have been recommended, the same spirit of scepticism has prevented their application.

The conflict between the two views is nowhere so perplexing as when the physician himself happens to be the sufferer. Even to-day we meet with members of the profession who prefer the disease to the irksomeness of its cure. They are the exception, whilst the name is legion of those physicians, with less authority than Sydenham,

but likewise martyrs to the gout, who are strong believers in treatment, and who on no account would approve in their own case of the adoption of an expectant plan.

Lastly, *idiosyncrasy* adds many a complication. The patient who is an expert in the knowledge of his own familiar symptoms, and of the influence of various remedies, is often fully aware of the peculiar effect which some of them may take upon him. In short, the confirmed gouty subject entertains more commonly than any other patient settled views as to treatment, and the physician may be wise in not too lightly disregarding his opinion.

#### CHAPTER XXXVII.

# THE PRINCIPLES OF TREATMENT, AND THE THERAPEUTIC INDICATIONS IN GOUT AND GOUTINESS.

#### THE VARIOUS MODES OF TREATMENT.

THE treatment of gout may be classified as medicinal, dietetic, and hygienic. Of these three varieties the first is that of which we can speak with least certainty, and also that most apt to vary with the subject or the stage of the affection. A review of the medicinal agents and of other therapeutic measures, and of their mode of employment in gout, will form a necessary introduction to this part. The treatment of acute gouty arthritis, of chronic gouty arthritis, and of retrocedent gout, will be considered; and we shall deal finally with the treatment of goutiness, with that of its chief manifestations, and with its prophylaxis.

## THE PROSPECTS OF TREATMENT AT VARIOUS STAGES.

Some cases of inherited gout, beginning in youth and running through a long life, present us with an almost complete series of the phases of the affection, including the early symptoms of goutiness, the acute attacks which may be complicated with retrocessions, and chronic gout, with its arthritic changes and visceral symptoms, and with its characteristic fluctuations under the influence of the seasons.

The longer the gouty tendency has existed, the more does it become confirmed and intensified: not that there is more of the acute character about it, but because the whole constitution is more inveterately gouty. In a few cases, a maximum may be touched about the period of middle life, and although gout may never be absolutely thrown off, it may gradually need less of the physician's attention and of any systematic treatment except the hygienic. With increasing age it may be almost regarded as obsolescent.

In gout the results of treatment are often difficult to estimate. This is due to the waviness, to the flux and reflux in the incidents of the affection, which, it would seem, spontaneously tends to periodical or to irregular aggravations and remissions.

Success, during the earlier stages, will greatly depend on the adequacy of the measures recommended, and yet more on the thoroughness with which the patient lends himself to their application. With sufficient care, and in the absence of accidental complications, the worst evils of gout might be indefinitely staved off.

So long, however, as the gouty tendency prevails, any unlucky circumstance, such as a surgical injury, which may suddenly remove the protecting effect of regular and full exercise, may lead to an outbreak. This danger may be partly met by forethought and by judicious management of the patient thus unhappily condemned to muscular inactivity.

It is in the earliest stage that the best results can be obtained. The advantages of a systematic preventive treat-

ment should be secured at the earliest age for those children whose family history points to a likelihood of gout being ultimately developed in them. If their delicacy be successfully combated, much of the tendency to visceral changes described in connection with goutiness may be held in check, and the serious visceral consequences apt to result from their continuance will be prevented, with considerable improvement in the prospect of life. It is clear, however, that nothing can raise the resistance of the subjects inheriting a tendency to gout to the level of that of the robust. The avoidance of gout must be for them a lifelong study. In the words of Sydenham: 'As for a radical cure, one altogether perfect, and one whereby the patient might be freed from even the disposition to the disease—this lies, like Truth, at the bottom of a well; and so deep is it in the innermost recesses of Nature that I know not when or by whom it will be brought forward into light of day.'

## THE THERAPEUTIC INDICATIONS IN GOUT AND GOUTINESS.

The Remote 'Causal' Indication.—As in all other affections, the indications for treatment are based upon a consideration of the cause, and a study of the phenomena and of the symptoms. Both gout and goutiness differ, however, from the majority of ailments by possessing, in addition to the stage of activity, a prior stage of latency, or stage of evolution.

The original cause of gout was correctly appreciated by Greek and Roman physicians. This portion of their therapeutics leaves little room for improvement. It includes such orthodox precepts as the avoidance of all excesses, a regular and frugal diet, exercise, etc. These

remote causal indications, sketched out for us by our distant predecessors, will be our guide in the subject of hygiene and of diet. They are identical with the indications of *preventive* treatment. In this resides their greatest practical importance.

The Proximate Causal Indications.—Declared gout also claims to be treated on the rational basis of its immediate causation. Here we realize the helplessness of our pathology. With every change in the ætiological theories of gout the methods of treatment have presented corresponding oscillations, and extreme and exclusive measures have been their outcome. We are still imperfectly acquainted with the ætiology, and we cannot yet boast of having fulfilled the causal indication in the treatment of gout.

The objective indications are furnished by a clinical study of the phenomena themselves, irrespective of their cause. Accurate observations, clinical instinct and experience, and practical wisdom should be sufficient guides. Yet in framing their treatment of the obvious phenomena physicians have not wholly succeeded in divesting themselves of their theoretical notions as to causation. Clinical indications have not always been followed with an open mind, and on the pure lines of common-sense. Pathological views as to the nature of inflammation, apart from gout, have also cast their shadow upon the practical treatment, which otherwise might have presented greater uniformity.

These shortcomings are illustrated by the history of the topical treatment of gout, which presents almost as great a variety as that of its internal medication. Every kind of agent has been prescribed and applied heat and cold; the cautery or moxa and ice; leeching and scarifying; blistering and astringents; soothing applications, such as oil, and stimulating lotions; so divergent were the views which have been held of the nature of the local trouble.

Symptomatic Indications of Treatment.—Lastly, under this heading would naturally fall the indications arising out of the patient's conscious feelings, and also those derived from obvious clinical features, such as aspect, fever, and the various constitutional states. These indications are of special importance in connection with goutiness, many of the manifestations of which are rather symptomatic than objective; but in gout also they correspond to a definite part of our therapeutics.

#### THE SPECIAL INDICATIONS IN GOUT AND GOUTINESS.

Sydenham's ideas of the therapeutical indications were governed by his pathological views: 'In respect to the treatment, if we look to the humours themselves, and the indigestion from which they arise, it seems at first that we have to evacuate the aforesaid humours, and to guard against their increase by strengthening the concoction, which is only what is to be done in all humoral complaints. In gout, however, it seems as if it were the prerogative of Nature to exterminate the peccant matter after her own fashion, to deposit it in the joints, and afterwards to void it by insensible perspiration. In gout, too, but three methods have been proposed for the ejection of the causa continens—bleeding, purging, sweating. Now, none of these succeed.'

Garrod's identification of uric acid as the chief part of the *materia peccans* has clearly defined the indications. In dealing with uric acid as the alleged basis of gout, three lines of treatment lie before us—the preventive, the eliminative, and the antidotal; and these we shall have to follow out in connection with goutiness, and with acute and chronic gout, whilst the hygienic and prophylactic treatment to which we have referred meets the indication of the *remote causation* of gout.

In goutiness or threatening gout the leading indications for treatment are supplied by the acidity, by the lithæmia, and by the inertia of the excretory functions; and the same apply also to the preventive treatment of gout. On all these points, except in relation to acidity, our practice differs from that of Sydenham. We should promote free action of the liver, of the bowel, of the skin, and of the kidney, as well as obviate the acidity. The manner in which these indications are to be carried out will be explained further on.

Meanwhile, the ætiological factor should not be overlooked, and if gout is rightly to be traced to a deficient activity of the oxidizing processes, the practical conclusions are obvious.

In acute gout the indications are local and constitutional. Our ignorance of the mechanism of the attack, and the unaccountable manner in which metastasis may occur at times, limit our action. Of one thing we are sure—that a gradual relief of the gouty symptoms by mild measures is never attended by evil complications, but that their sudden repression, particularly by external applications, has its risks.

Local pain should, if possible, be mitigated by local treatment. Its relief by strong sedatives is not at present available, unless colchicum be classed among the latter. Opium and morphia are contra-indicated, since they check the secretions.

The swelling and arthritis are meanwhile relieved by the internal medication, and by those local measures which allay the pain.

The constitutional indication connected with uric acid is fulfilled by the derivative treatment directed to bowel, kidney, and skin.

Lastly, the other aspect of the ætiological treatment is carried by the restriction of the diet to those foods which may be digested without effort, without acidity, and without adding much nitrogen to the accumulated excess.

The chronic stages of gout are to be managed on almost identical lines, both as regards medicinal treatment and hygiene. Unhappily, the capacity for movement is often greatly restricted, but we now possess fairly good substitutes for active exercise in passive movement, massage, and resistance movements.

The local treatment of tophaceous gout would aim at the removal of the accumulations, and particularly at checking their growth. Both these ends are difficult to secure. Surgical interference has not hitherto had much success. The solvent treatment by alkaline applications meets with more approval, and is undeniably sometimes of use. The future developments of electricity may perhaps yield better results from a cautious application of the principles of electrolysis than from any other method. Our most anxious care should be to preserve as much motion as possible without setting up dangerous irritation in the joint.

In gouty cachexia, and in the complications, cardiac, renal, diabetic, etc., of chronic gout and of goutiness, fresh indications are superadded to those special to gout. There are stages in advanced gout and in its organic consequences in which all hope of amendment must be abandoned, and palliative treatment only remains. The earlier periods, when the articular disease is not complicated with visceral degeneracy, are more promising.

The indications of preventive treatment have been sketched out in the foregoing; they apply with special force to the management of the progeny of gouty parents. Childhood and youth are the time when an impression can be made upon the inherited weakness, and the measures of hygiene which have been advocated in gout and goutiness can be carried out with the most beneficial results.

#### CHAPTER XXXVIII.

#### THE THERAPEUTIC METHODS AND AGENTS.

## THE EVACUANT METHODS.—I. EMETICS AND PURGATIVES.

Emetics.—The administration of emetics for gout, apart from its bronchial or gastric complications, has fallen into disuse, and is not likely to be revived. Any office they might have fulfilled is well and easily accomplished by other means.

Purgatives.—Properly handled there is no better method for the relief of gout and goutiness than gentle purgation. This had been recognised by some of the ancients. Sydenham gives for his strong disapproval of it reasons which are full of instruction.\* The paradox of his adverse

\* 'Then as to any catharsis, either above or below, we must remember that it is the inviolable rule of Nature, interwoven with the essentials of the present disease, to throw the peccant matter upon the joints. If so, all that can be done by purges or vomits is to throw what Nature would ingest through the extremities into the blood. Hence it happens that what was meant for the joints, takes hold of one of the viscera; then the patient's life is in danger. . . .

'Sure am I that all purging, mild or sharp, intended to relieve the joints is mostly injurious, whether it be during a fit, to diminish the peccant matter; at the end of one, to dissipate the remnants of the disease; or during an intermission, to guard against the occurrence of one. . . .

'In the first place, if given during the fit, they interrupt the work of Nature. . . . After a fit, a purge should perhaps be given to work off the remains of the disease. It will just bring on a fresh one, equally

attitude is rendered more striking by the following admission: 'Nevertheless, this method, bad and mischievous as it is, has made the reputation of many empirics, who, nevertheless, have made a secret of the purge they use. For it must be noted that whilst the catharsis goes on, the patient either suffers not at all or very slightly; and provided that it can be kept on for a few days, if no fresh fit supervene, the original one will go off. Sooner, however, or later, he will pay a tremendous penalty arising from the disorder into which Nature has been forced headlong by the aforesaid agitation of the humours.'

To differ from Sydenham is less unsafe when we find his opinion at variance with his observations. Our object is to keep the materia peccans from the joints, and to protect them from its irritating effects; and in carrying out that endeavour no time is to be lost. Though it is now generally understood that the disease cannot be cut short even by excessive purgation, and that great harm, nay, danger, may arise from this form of jugulant treatment, moderate derivation through the intestine is the most effectual means at our disposal. The amount of benefit to be secured will greatly depend on the way in which this indication is carried out.

Purgation viewed as Part of the Hepatic Treatment.—The mild initial purgation is in reality a first instalment, which needs to be followed up, in the 'hepatic' treatment of acute gout. The drugs now in use carry out this essential indication in a manner not attained in the days of Sydenham. This may explain the less favourable results of the purgative treatment in his hands.

bad. . . . This I have found in my own person. . . . Lastly, in respect to purging at certain intervals, whilst the health is good . . . it must still bring on one, and that for reasons already given. If it fail in doing this it by no means carries off the disease.'

#### II. BLEEDING.

This ancient method of elimination is not now regarded with favour, and is recommended neither by the probabilities nor by the results of its employment. Others besides Sydenham had spoken adversely of its action in gout; the latter, however, recognised it as part of the treatment of the complications of pneumonia and of congestion. At the present time the indication for venesection arises less often than ever before. Local depletion is also in most cases undesirable and unnecessary.

#### III. DIURETICS.

Derivation by diuresis is, from the standpoint of the uric acid theory, the most rational of methods. obvious requirement is to eliminate the uric acid through its normal channel of excretion. In practice the indication of increasing the flow and the solvent power of urine is always carried out by the substitution of a fluid diet for solid alimentation. Colchicum also frequently acts as a diuretic. The use of the stronger diuretics is not, however, desirable; some of them, such as digitalis, which raise the blood-pressure, are contra-indicated. The kidney itself is in a tender state, and should not be over stimulated. No risk of this kind attaches to the use of the alkaline salts of the organic acids, and particularly to the bicarbonate, citrate, tartrate, and acetate of potassium. They possess also the advantage of rendering the urine less irritating to the kidney, whilst promoting the solubility of urates.

#### IV. DIAPHORETICS.

Diaphoresis, a much less powerful method of derivation than those which we have just sketched, is, like other agencies which effect little at any one time, but much by their continued action, eminently suited to the treatment of goutiness, and of the subacute gouty state. Sydenham recognised its value in the intestinal complications: 'If, notwithstanding the laudanum and the exercise (the first remedy to which we must resort in diarrhæa), the bowels be still purged, and the purging be accompanied with gripes, etc., the only remedy known to me is a sweat, brought on by the appropriate medicines. . . . In this way I cured myself, some years ago, after I had imprudently thrown myself in the way of danger by having taken cold water as my ordinary drink, and that after I had sought help from cordials and astringents in vain.'

Diaphoresis is also of great service in acute gout so long as, by a proportionately liberal supply of fluids, the urine is kept thoroughly diluted. Indeed, it fulfils a valuable office in connection with acute arthritis by relaxing the arterioles of the skin, and considerably lowering blood-pressure. Theoretical objections probably explain Sydenham's distrust of its use:

'The evacuation of the peccant matter by sweats, although less mischievous than the other two forms, is still prejudicial. . . . Hence in gout, as in all other diseases where the sweats . . . are forced rather than natural, it is very dangerous to bring them on too violently, and solicit them beyond that degree of concoction to which the humours requiring an elimination have arrived of their own accord. So teaches Hippocrates: "Cocta non cruda, sunt movenda et medicanda."

We agree with this caution. Little could be gained by excessive diaphoresis to compensate for the lowering effect on the patient; but its moderate degrees are a source of comfort, and truly beneficial.

#### THE ANTIDOTAL OR NEUTRALIZING METHOD.

This indication was clearly perceived by all humoralists, but their erroneous conception of the nature of the offending matter defeated their intentions. Sydenham's peculiar views as to its proper disposal led him into the following dilemma:

'If evacuants are out of place in gout, what are the indications of treatment? Two points are most particularly to be considered. The first is the causa antecedens, or the ingestion of the humours arising from a defect of spirits. The other is the causa continens, or the heat and exæstuation of the same, when, from their prolonged delay in the body (a delay arising from the aforesaid inconcoction), they have become putrid and acrid. These two are as far as the poles asunder. What helps one hurts the other. Hence the difficulty of treatment.'

The progress of chemistry, and the identification as part of the materia peccans of an excess of acid, and specially of uric acid, have solved this dilemma, and rendered possible a rational application of the antidotal method. The latter, in association with the uric acid theory, has claimed ever since growing and almost exclusive attention.

The alkaline treatment alluded to above (cf. p. 341) will be further considered later on. Sir W. Roberts has shown that some of the chemical activities which had been attributed to the salts of the alkaline metals are imaginary. Meanwhile, as though to remind us by a reductio ad absurdum that the neutralizing and solvent treatment is only a secondary indication, organic substances of great alkalizing power have lately been tried, which, had they proved sufficiently stable, might have produced in the economy results less desirable than the mere solution of

uratic deposits. To these organic solvents we shall make further reference.

It has happily been shown that alkalies are not the only antidotes of uratic gout, and that the precipitation, and even the formation, of uric acid may be to a certain extent controlled by other checks than that of an alkaline reaction.

#### THE PREVENTIVE METHOD.

This is the absolutely rational method, easier to recommend than to adopt. To obviate the production of an excess of uric acid and of acidity, and a precipitation of the former, diet and hygiene are the direct means, and upon them we shall dwell in due course.

#### THE LOCAL METHODS.

The practical aspects of local treatment will be dealt with in subsequent chapters, and call for few remarks at this stage.

Warmth and Cold.—The simple clinical experiment constantly performed in the test-tube—that of dissolving the uratic sediment by gentle heat—might almost be adduced an an object-lesson in therapeutics. Moderate and equable warmth is of undoubted value in the treatment of gout, and a source of comfort; still, it does not appear that warmth is in itself curative, nor is it strictly preventive. At any rate, experience does not justify the conclusion that cold per se will lead to gout.

Sir A. Garrod, however, believes in a local predisposing influence of cold. Tophi would attack the ears because much exposed to cold; whilst those of women would suffer much less because more protected. Again, the toes and the knees would be liable to gout because often cold; the hips would remain exempt because sharing in the tempera-

ture of the trunk. The practical conclusions to be drawn from these facts are obvious.

Anodyne applications are the main indication for the relief of pain. No objection can be raised against their help, which is increased by warmth.

Resolvents and Astringents.—The alkaline applications are the representatives of the first of these groups, and when of suitable strength and composition, they are beneficial, both in acute gout and, with a special view to their solvent action, in tophaceous gout. Astringents need delicate handling. They answer best in combination with anodynes, and moisture.

Local stimulants have little to recommend them in the treatment of gout beyond the fact that some patients find relief in their application, and believe in them.

Local depletives and revulsants, such as leeching, scarifying and blistering, on the one hand, the actual cautery and the moxa, or immersion into cold water, on the other, have ceased to form part of our therapeutic methods.

#### CHAPTER XXXIX.

#### THE MEDICINAL AGENTS .- COLCHICUM.

# HISTORY AND GENERAL PROPERTIES OF COLCHICUM.

THE history of the medicinal treatment of gout begins in earnest about 580 A.D. with the introduction by Alexander of Tralles of the drug termed 'hermodactyl,' perhaps identical with that derived from the East in more modern times, and regarded by Pereira as having consisted of the corms of some species of Colchicum autumnale, and by others as having been a variety of Colchicum variegatum. Hermodactyl was freely employed during the Middle Ages by the great Arab physicians (Avicenna, Serapion, etc.). We may infer that it partook, though in a milder degree, of the properties of the drug now in use. On this assumption, the interval which may be termed the colchicum period would have been a very long one; but the more limited period of the employment of Colchicum autumnale and of its great vogue was that of the fifty years which followed Storck's original communication: it is identified with the names of Home, Armstrong, Scudamore, Williams, and others.

Before Storck had the boldness, in 1763, to try its effects in his own person and in that of patients apparently hopelessly stricken, *Colchicum autumnale* had been regarded

as a dangerous poison. Since then it has often been the subject of experimental study, and its clinical employment has afforded continual opportunities for a discovery of the secret of its power, but in vain. Our knowledge does not extend much beyond its elementary pharmacology. The dried corms and seeds of the meadow saffron contain—besides tannic and gallic acids, starch, sugar, gum, etc.—an amorphous, yellowish, bitter alkaloid, colchicine, C<sub>17</sub>H<sub>19</sub>NO<sub>5</sub>, which is readily soluble in water and in spirit.

According to Mitchell Bruce,\* colchicine depresses the convolutions and the spinal cord, causing loss of sensibility and of consciousness, and diminished reflex excitability; the peripheral sensory nerves being also paralyzed, whilst the motor nerves and the muscles are unaffected. The activity of the respiratory centre is lowered, so that death occurs by asphyxia, and the heart weakened, so that the pulse may become intermittent, perhaps as a disturbance secondary to that of the respiration; the skin perspires, and the amount of urine is diminished,† but 'the uric acid, and probably the urea, are increased in quantity,' the kidneys being found hyperæmic after death. As a gastro-intestinal irritant, colchicum sets up vomiting and purging, the stools being bilious in character.

It is remarkable that our knowledge of the value of the drug should have come so late, and that it should have remained *empirical*. No less striking is the fact that the modern growth of chemistry and of pharmacology, which have furnished us with new remedies of great efficacy in some other ailments, should have left colchicum in

<sup>\* &#</sup>x27;Materia Medica and Therapeutics,' p. 398, 1891.

<sup>†</sup> Dr. M. Bruce informs me since these statements were written that he has repeatedly observed considerable diuresis coinciding with the rapid relief of the acute attack by colchicum.

undivided possession of its reputation as the specific in gout.

The toxic effects observed in man comprise vomiting, purging with tenesmus, a feeble and a slow pulse with cold extremities, and great prostration. The mucous membrane of the stomach and of the intestine has been described as much inflamed, ulcerated, and even 'gangrenous' in cases of poisoning by the drug.

In Sir Everard Home's experiments, the injection of colchicum wine into the jugular vein of dogs produced vomiting and bilious diarrhœa. The breathing was remarkably slowed, and the pulse was likewise slowed and depressed in strength, but later it became very rapid and irregular. After death the mucous membrane was congested and inflamed almost throughout the intestinal tract. These results would point to a decided influence of the drug in three directions—heart, alimentary canal, and liver; and the same influences may be followed out in the accounts given of its action in therapeutic doses, viz., depression of the pulse, purging, rarely, however, vomiting, though nausea is the common complaint after the full dose.

The beneficial effects in gout have been variously attributed to the same influences; that, however, which was first noticed and described was the action on the kidney. The marvellous recoveries from dropsy which Storck relates were in each case accompanied with the passage of 'vast quantities of urine'; they led him to regard the drug as essentially a diuretic.

This alleged diuretic action has not been recognised in the same degree by most observers; many have failed to find any diuresis whatever, and it has even been stated by some that the urinary flow was diminished.

This want of unanimity, this positive contradiction in

the results of separate observers, in spite of a careful study of the effects produced on the urine, and the absence of any marked changes in the quantity, in the quality, and in the constituents of the secretion, have special significance when contrasted with the energetic action of the drug upon other organs and functions.

It would seem difficult to ascribe so great a relief as that obtained in gout to the operation on the kidney of subtle and hardly recognisable influences, whilst in other directions the economy is being searched by the violence of the remedy. Graves was probably conscious of this inconsistency when he sought to explain the beneficial action of colchicum less by a diminished renal excretion of uric acid than by some check on its formation in the organism.

Esterlen was unable to find any alteration in the amount of urine secreted, or in its percentage of urea and of uric acid. Baecker\* was rather inclined to admit a diminution of the relative amounts of both substances. Chelius, on the other hand, has reported a decided increase in the output of uric acid.

Lecorchét publishes the following results of his administration of the tincture of colchicum (20 to 40 drops in twenty-four hours) in cases of gout and rheumatism: As regards (1) the amount of urine secreted, no definite conclusions could be drawn from the varying individual observations. (2) Reaction: In all cases the acidity was markedly reduced. (3) Urea: No definite conclusions could be drawn. (4) Uric Acid: In the rheumatic cases the quantity was irregularly increased or diminished; but in both cases of gout submitted to the treatment the uric acid was diminished. (5) Phosphoric Acid: No definite

<sup>\* &#</sup>x27;Beiträge zur Heilkunde,' Bd. ii., 1849.

<sup>† &#</sup>x27;Traité Théorique et Pratique de la Goutte,' Paris, 1884.

conclusions were warranted by the slight and varying modifications noted. (6) Potassium, Sodium, Calcium and Magnesium: In another series of observations conducted in three cases of rheumatism and of rheumatoid arthritis, there was found a very marked increase in the excretion of potassium, and a much less important increase in the sodium of the urine. The calcium and the magnesium were both diminished.

Of the various functions which have been supposed to be influenced by colchicum, that of the kidney is obviously the least affected.

Sir A. Garrod's\* conclusions from his extensive observations on the influence of colchicum on the urine are to this effect: (1) 'There is no evidence to show that colchicum produces any of its effects upon the system by causing the kidneys to eliminate an increased amount of uric acid; in gout, when the drug is continued for any lengthened time, it appears to exert a contrary effect.' (2) 'We cannot assert that colchicum has any influence upon the excretions of urea, or of the other solid ingredients of the urine.' (3) 'Colchicum does not act as a diuretic in all cases; on the contrary, it often diminishes the quantity of urine, more especially when it produces a marked effect upon the alimentary canal.' And again: 'It is asserted by some that colchicum possesses the power of rendering the urine neutral, or even alkaline; that such is not an invariable effect, my own observations prove.'

It is more than probable that *individual peculiarities* partly explain the difference in the renal effects noted by the same observers at different times, as well as the conflicting statements of separate authorities. At any rate, the evidence in support is not sufficiently conclusive to

<sup>\*</sup> Loc. cit., p. 334.

enable us to regard colchicum as strongly modifying the renal function. Again, on the constitution of the blood, we are not in a position to trace any definite action—if, indeed, any such exist.

# MODE OF ACTION OF COLCHICUM AS A SPECIFIC IN GOUT.

So far, the evidence as to the mechanism of relief is practically negative.

Three directions remain in which we might seek the desired explanation of the relief given in gout: The cholagogue and purgative, the nerve-depressing, and the heart-depressing property. Most probably the specific value of colchicum resides in their happy combination. Each separately would fail to relieve; united in a happy proportion, as they are in colchicum, they succeed. This view is suggestive; if correct, it might render us more hopeful of imitating the prescription of nature by artificial combinations, whilst opening up novel aspects of the pathology of gout.

Which of the properties in question is most to be credited with the result it is impossible to say, since we are not even certain as to their mechanism. Whether we turn to any purely sedative or to any purely aperient property, the argument employed by Sir A. Garrod applies with equal force. There are other purgatives and other sedatives more potent than colchicum, yet they will not check the disease as colchicum does.

Again, a purely *nervous* influence must not be left out of consideration; the nervous system is rapidly brought under the action of any soluble principle introduced into the blood, and must experience its effects for good or for evil. But it would be too large a postulate to suppose that

colchicum possessed a local and specific action upon the hypothetical medullary centre for articulations first introduced to our notice by Dr. Buzzard.

Of any essentially anodyne virtue in colchicum analogous to that of opium, we know nothing, and this possibility may be almost excluded. We are compelled to look to other well-marked properties of the drug, and particularly to its cardiac and hepatic effects.

The Gastro-Intestinal Action.—The powerful immediate action exerted on the gastro-intestinal mucous membrane has already been described; it forms, as it were, the central and most tangible feature in poisoning by colchicum. The purgative action is not the earliest in the case of moderate doses; but it is regarded as the first indication of commencing gastro-intestinal irritation, a result of the drug which we do not seek in gout. A feeling of nausea is the full extent of the physiological effect which we desire to secure, and this is also practically the sign that the full therapeutic value has been obtained from the remedy.

The Cholagogue Action.—A reasonable theory is that which has attributed the relief conferred by the drug to its marked cholagogue property, as fulfilling one of the most important indications in the treatment of gout—the stimulation of the secretion of bile. Colchicum has been shown by Professor Rutherford to be one of our most active cholagogues. Here, again, we do not lose sight of the interactions which probably occur between mucous membrane, nervous system, and circulation. A great deal may be brought about in sympathy with the local gastro-intestinal stimulus, the hepatic effect itself partly depending upon the latter.

The Action on the Circulation.—A very definite vascular relief, partly realized by the patients themselves, is un-

doubtedly obtained. Colchicum not only slows the pulse but depresses its strength—a remarkable contrast with the action of members of the digitalis group, which slow the pulse, but increase its strength, and with those of the atropine group, which diminish the strength whilst increasing the frequency.

That a great part of the vascular results may be also merely reflected from intestinal irritation is rendered likely by the fact that in animals, when the drug is injected directly into the circulation, the heart and the blood pressure are only slightly altered.

Reasons might be found for attributing the sedative action on the sensorium and on the peripheral nerves to circulatory changes. If the latter are brought about through the influence of a vaso-motor reflex, then the sedative effect would be secondary to the local action on the mucous membrane. For this surmise we have the support of clinical experience, in so far as the dose that most relieves is that which verges on the production of gastro-intestinal irritation.

Morphia, which relaxes the arterioles and diminishes the tension without at first markedly influencing the rate, is in this respect the nearest approach to colchicum, from which it widely differs in its remaining properties. As regards immediate relief to the painful symptoms, it might probably surpass the latter. Unfortunately, the alleviation is at best of limited duration, and, for reasons elsewhere stated, its continued administration is not conducive to the patient's ultimate recovery. All practitioners of experience are agreed as to the comparative failure of opium, and leave it aside in the systematic treatment of gout.

The mechanisms for the reduction of vascular tension also differ. Colchicum probably acts by counter-irritation

and by promoting various glandular secretions; morphia, by reducing the perception of irritation, whilst rather checking glandular activity. The contrast is manifested in the later physiological effects: morphia produces constipation, and checks other excretions; whilst colchicum is a cholagogue, and perhaps a diuretic.

The question thus raised, of direct importance in its relation to therapeutics, is worthy of consideration also in connection with the pathology of the vascular reactions of gout.

The cardio-vascular effects are the first to claim our attention. An observation of the local phenomena of acute gouts shows us a violent local vascular storm, turgid veins, paralyzed arterioles, the mysterious appearance of œdema, which reminds us of urticarial rashes or of the sting of insects. The pulse is tense and frequent, adding by its tension to the distressing pressure and pain felt in the inflamed part.

Cardiac depressants might be expected to mitigate these evils, and colchicum, which abates them 'like magic,' probably acts in this way.

The lowering of the heart's excitement, and of the strength of beat, is at once felt as an instalment of relief. The lulling of the pain may not be so rapid as with morphia or an anæsthetic, but it is more lasting, because, under the influence of colchicum, derivation takes up the work begun by the general vascular sedative action, and by the local relaxation of the blood-pressure.

According to this view, the alterative and the hepatic properties of colchicum would actively co-operate with its vascular depressing effects. We find a parallel to this supposed mode of action in the pacifying influence exercised on the restlessness and discomfort of infants by small doses of calomel or of grey powder—an influence so marked that it has suggested the view that mercury might act as a hypnotic.

Haig connects the beneficial effects of colchicum with its influence on the excretion of uric acid. He recognises in colchicum an action analogous to that of some of the metals, which induce primarily a retention of uric acid with aggravation of gouty pains; but soon intestinal irritation is set up, accompanied with a fall of urea and of acidity, and uric acid is discharged.

The power of colchicum to render the urine neutral, or even alkaline, was not borne out by Garrod's observations.

Sir Dyce Duckworth is of opinion that 'a large part of the beneficial effect of colchicum in gout is due to its decided action on the liver. Powerful cholagogue action necessitates active hepatic metabolism, and with this is secured a more complete disposal of uric acid and other products, which are believed with good reason to be retained in the liver in cases of gout.'

In conclusion, though we have insisted upon the cholagogue and vascular sedative virtues of colchicum as the most likely agents of relief, we should be ill warranted in excluding its other properties in forming an opinion as to the mechanism of the relief. Our impression is that the merits of the drug may reside rather in the finely-adjusted combination of its qualities than in the isolated strength of any one of them. Their delicate balance may be just measured for the work needed, and may constitute a specific aptness which no other distribution of power could reproduce.

If colchicum is of remedial value in the chronic stage of gout—and on this point we have a consensus of opinion—

if, moreover, it possesses a preventive value when administered during the interval—and this view has been largely held—the conclusion is almost forced upon us that the mode of action is a complex one, since the acute stage where the relief is so marked entirely differs from all other stages of gout.

#### CHAPTER XL.

### COLCHICUM: ITS INDICATIONS AND CONTRA-INDICATIONS.

### THE OBJECTIONS URGED AGAINST THE USE OF COLCHICUM.

Whilst recognising the controlling power exercised on gouty inflammation by colchicum, various physicians of eminence have been impressed with the injurious effects of a continuance of the drug, or of its administration in large doses. This adverse opinion has been largely caused by the injudicious use made by the patients themselves of patent medicines, such as the Eau Médicinale, Wilson's Tincture, Reynold's Specific, and Laville's Tincture. Scudamore strongly deprecated the use of the Eau Médicinale, though he approved of the careful administration of colchicum. Todd, however, was a decided opponent of the latter, and is largely responsible for the bad name which has been attached to it.

The following definite objections have been formulated:

- I. Even in the absence of the vomiting and of the diarrhœa, sometimes of a severe and persisting kind, which indicate gastro-intestinal irritation, the drug is apt to produce a degree of nausea, depression, and languor, which seriously detract from the value of the relief to the local symptoms, and lay the patient open to their almost immediate return.
- 2. If persevered with, it lowers the vitality, and exposes the patient to chronic gout.

3. A long continuance of the treatment establishes what has been termed the *colchicum habit*, viz., a tolerance for the drug and a worse form of gout, peculiarly refractory to this as well as to other remedies.

With regard to the first objection, there is no doubt that some subjects are unusually susceptible to the action of the remedy, and entertain a strong aversion to it, based upon an experience of its depressing effects. In many of these cases the drug was probably less to blame than the mode of its administration. To this we shall presently revert.

The second objection, viz., that the use of colchicum tends to change acute articular into torpid visceral gout, is hard to disprove, but equally difficult to prove. Rendu finds an argument against it in the number of those who have never suffered from visceral gout, but from frequent acute attacks, in spite of the use of Laville's tincture or Lartigue's pills.

Considerable weight should be attached to the testimony of such competent authorities as Sir Thomas Watson, who was a firm believer in the advantage of a systematic course of colchicum, and of Sir A. Garrod, who also advocates its employment.

Lastly, the 'colchicum habit,' according to Todd, is one easily acquired, whilst the drug thus abused loses its effect for good, but not that for evil. He gives the famous instance of a lady of rank—a colchico-maniac—who ultimately died of prostration after the prolonged use of colchicum in 100 minim doses. Todd never prescribed it in old age or asthenia, used it in small doses only (10 to 15 minims of the wine or 1 grain of the extract), and preferred, even in the case of strong subjects, to forego its aid, if possible, believing that, whilst shortening the attacks, it also shortened the interval between their recurrences.

Few physicians will be found to recommend the continuous and protracted use of so potent a remedy. Nevertheless, this practice has been occasionally adopted without detrimental results. Sir Henry Holland once administered it for two years consecutively with decided advantage. The patient, however, was also taking quinine. With this drug, more than with most others, individual susceptibility is a guide to medication.

Lecorché holds that, although it is a specific rather for the acute arthritic or visceral gout than for the gouty habit, it may be used continuously as an anti-gouty remedy; but the doses should be smaller, in view of the possibility of membranous enteritis being set up.

Galtier-Boissière (quoted by Lecorché, *loc. cit.*, p. 603), taking the same unfavourable view as Todd, has recommended its use in very small doses and on alternate days. Lecorché condemns so pusillanimous a use of the remedy, which should be given boldly, though not long continued. He shares in the belief in the drug expressed by Scudamore, Graves, Watson, Garrod, Gairdner, and others; and he holds with Graves that the formation of uric acid is lessened by its use, which also restrains within cells that undue tendency to dissociation which he regards as characteristic of gout. Of its superiority over sodium salicylate he entertains no doubt, and he considers it to be a more rapid, as well as a safer, remedy.

THE INDICATIONS OF COLCHICUM, AND THE MODE OF ITS ADMINISTRATION, CONTINUOUS OR INTER-MITTENT, IN LARGE OR IN SMALL DOSES.

The indications for a vigorous use of colchicum are much less common than they formerly were. The violence of the acute attack is less, and the remedies for its relief have been multiplied. In chronic gout we trust more

than ever to hygienic and dietetic measures and to medicinal agents, such as the iodides or the salicylates, which act more slowly, but can be long continued.

Sir A. Garrod regards acute gout as the chief indication for its employment. In chronic gout it should be given only during the acute exacerbation, and then with great care. During the intervals it may be occasionally prescribed 'as a cholagogue in lieu of the preparations of mercury.'

The continuous use of the drug is based on a belief in its power to ward off attacks; but this mode of administration defeats its own ends. The opponents of colchicum have done service to the cause of its proper and well-regulated use by showing that a tolerance of the drug is above all to be avoided, not so much in connection with any direct toxic danger, as with the eventual loss of an advantage. There is, however, an impression that colchicum may be sometimes cumulative. This would, if confirmed, be an additional argument against the continuous administration. This practice is not likely to find favour with the physician, but will probably still be carried on by some of the patients who manage their own case.

The intermittent plan is that best suited to the disease and to the remedy. On the grounds of a distant analogy with digitalis, much may be said for the intermittent use of the drug when employed (as in the acute attack) as a vascular sedative. In digitalis there is also a secondary or later action, that on the kidney, which it may not in all cases be necessary to elicit or to keep up. Similarly with colchicum, it may be wise to be content with the relief given by the early doses, and not to wear out the efficacy of the drug by its constant administration.

Full doses, followed by smaller ones, are an advantage.

This method, which also has its analogy in the occasional practice of giving large single doses of digitalis in heart disease, provides a full force of the remedy at the time when it is most needed, and when any depression it may produce will be least resented, whilst subsequent doses may be kept relatively small, and free from much risk of disagreeing with the patient. Sir A. Garrod recommends half a drachm to a drachm of the wine at starting, and subsequent doses of 10 to 20 minims twice or thrice daily. He believes in keeping up the effect in a mild and diminishing degree for several days after the inflammation has subsided.

Simultaneous purgation with the first large dose by means of a suitable saline is an approved and practical plan; it is advocated by Sir A. Garrod. The immediate effect of the dose of colchicum is partly obtained, but its aftereffects are avoided, and much smaller doses will then suffice to carry on the action. The same authority condemns the use of colchicum, in the larger doses, as a purgative.

The dose of the wine of colchicum will vary with the patient's condition and age, and will be partly determined by the pre-existing state of the bowels, and by any pre-liminary measures, especially purgative, which may have been taken. When administered three or four times a day, 15 minims, in combination with salts of magnesia or with citrate of potash, will generally be amply sufficient, and the dose may be reduced to 10 minims. Alternative amounts will have to be regulated on this average basis. The guide to the amount to be administered is the reaction of the patient as regards the pulse, the nervous system, the bowels, and the skin; it has already been stated that the diuretic action of colchicum is subject to variations.

The nervous indication of approaching relief is the

diminution of pain and relative comfort sometimes obtained. The symptoms of intoxication are the depression, the faintness, or even tremulousness, which follow excessive doses, and are accompanied with undue depression of the pulse. The cutaneous indication of relief is gentle perspiration, which, however, is not always induced; that of the toxic dose is a clammy cold sweat.

As a rule, the *intestinal effect* acts as a premonitory indication of any untoward results in other directions. It is noteworthy that colchicum purgation does not in most cases set in till after some relief to the pain has been obtained. This, of course, does not invalidate the view that relief from the pain is ultimately an outcome of the action on the liver.

It is impossible to determine the value and the action of any vegetable principles possibly contained in colchicum over and above the alkaloids; nevertheless, various selective powers must be recognised as existing in plants, and, in this instance, we are quite familiar with definite properties of the drug, and especially with that relating to the secretion of bile. A common-sense view would be to attribute to the physiological effect on the liver the apparently proportionate result which is noticed in the relief of the gouty symptoms; in no other directionexcept that of gastro-intestinal irritation and of toxic nerve and heart depression, all of which are adverse to the cure of gout-do we find any action so definite and considerable as the cholagogue action insisted on by Professor Rutherford, who finds the bile not only more abundant, but more watery under its influence.

In prescribing colchicum, the slight differences in strength and mode of action between its preparations should be borne in mind. The tincture from the seeds, less commonly used, perhaps, than the wine of the corm, is about one-third more aperient than the latter. Again, in the relative activity of Battle's recent preparations, the liquor and the extract, slight differences may be found. The ammoniated tincture or compound tincture of colchicum is prepared from the seeds with sal volatile; it is much praised by some physicians.

As to the alkaloid *colchicine*, it may sometimes find application as a hypodermic remedy in minute doses  $(\frac{1}{50}$ th to  $\frac{1}{20}$ th of a grain) where special reasons exist for this form of medication. Such an emergency would, however, be extremely rare.

Sir Dyce Duckworth has also tried veratrine externally, and found it of some use where colchicine afforded none.

In administering the drug, we have the choice of two excellent methods. In the form of a pill the extract or the acetous extract may be given in varying doses, and with varying frequency according to the dose. Some practitioners prefer this more gradual and continuous action of the drug to that of the quicker-acting draughts; and the dry administration of the remedy is often convenient and grateful to the patient.

The opposite advantages are claimed for the fluid administration: the remedy is absorbed more quickly, and probably acts with greater effect. Most valuable, however, is the facility thus afforded of combining with it useful adjuncts. Among the latter, none, perhaps, is better than carbonate of magnesia, with or without a little sodium or magnesium sulphate, disguised by spirits of chloroform and peppermint-water, or some other carminative.

Veratria has rarely been given, and has proved unreliable and unsatisfactory. It possesses in a higher degree the faults which have been attributed to colchicum, without possessing its virtues.

#### CHAPTER XLI.

# OTHER MEDICINAL AGENTS.—THE ALKALINE TREATMENT.

THE TREATMENT OF GOUT WITHOUT COLCHICUM.

In spite of the reputation and of the value of colchicum as a specific, we are becoming more and more independent of its use. Is this a phase of fashion, or the outcome of altered conditions? Quite independently of the change which seems to have come over the type of the disease as manifested by the present generation,\* telling reasons might be suggested for this change in the tendency of practice.

So long as Sydenham's doctrine as to the harmfulness of purgatives held sway, colchicum was the more indispensable, because patients were largely dependent upon it for that hepatic relief which was ostensibly denied them by more direct means. In spite of theory, they ultimately secured from it their needful purgation. Hence, also, the popularity of various quack remedies compounded on the unerring lines of practical clinical results, which supplied it without stint.

A resumption of the use of direct hepatic purges at once robbed the specific of some of its employment. The larger doses ceased to be needed—nay, had to be avoided—their effects tending to discredit unfairly a most beneficial agent.

° Cf. p. 20.

To this circumstance may probably be traced the alleged uncertainty of its action, and the ever-recurring doubts and discussions as to its merits.

A ready welcome was thus assured to new remedies well backed with theoretical credentials from modern chemistry. The alkaline treatment was the first instalment of this promising supply, and so plausible a case could be made out in its favour, that it long held an imperfectly earned position in spite of clinical evidence. Indeed, although boldly convicted of clinical failure by the most experienced observers, it has only recently been shown by Sir W. Roberts to be based upon a chemical misunderstanding.

It is noteworthy that, although it was instituted long before the successes of the alkaline treatment of rheumatism, it received from them a powerful impulse. The same collateral influence was to repeat itself at a later date in connection with the brilliant achievements of the salicylic group. The pain of rheumatic arthritis was benefited in so striking a manner that the yet more painful arthritis of gout was expected to yield to the same influence. Hitherto, this hope has not been fully realized, but its partial gratification has been enough not only to give the new drug a place in the therapeutics of gout, but to supply with a powerful argument those who contend for a close kinship between the two affections.

To what extent the growing favour of the salicylates is to be justified in the future remains an open question. Dr. Haig holds that they will not have stood a fair trial until administered in the same large doses which alone are efficient in rheumatism—an experiment which practical acquaintance with the clinical uncertainties of gout has hitherto discouraged.

Moreover, the important group of gouty subjects, in

whom the renal function is disordered or the kidney deranged, could not be submitted to the treatment in question, even moderate doses of salicylate being sometimes badly borne by them. Idiosyncrasies in this respect cannot be ascertained beforehand, and cautious prescribing is necessary.

The idea of subduing the inflammation by neutralizing excessive acidity, the great argument in favour of the alkaline treatment, has been revived in support of piperazine, lysidine, and other alkaloids of considerable neutralizing power, which do not, however, modify the reaction of the urine in the proportion of their solvent power for uric acid in the test-tube. Piperazine has recently enjoyed a limited popularity probably not destined to endure.

The symptomatic treatment of the pyrexia and pain of gout by such drugs as phenacetin and antifebrin has also swelled the list of the modern substitutes for the treatment by colchicum; and the treatment by the benzoates has been chiefly applied to chronic gout.

In reviewing these methods of treatment, which have all found supporters, we are led to trace any reputation they may have gained to our inability even with colchicum to cure the attack immediately. Granted the delay in mending, which seems to be inherent to the acute gouty process, any remedy of sufficient authority may succeed in satisfying the patient and the physician so long as the preliminary relief has been secured which hygiene of the bowels and of the liver and diet invariably confer. The question as to the relative value of the various drugs is not solved thereby. We may gain an assurance as to their innocuity, but we obtain imperfect evidence of their efficacy unless they should be tested on the strict lines of experimentation. In the case of colchicum all doubts have long been set at rest by its almost unfailing useful-

ness under the most varied conditions of administration, and it will probably remain in continued possession of the high place it has long occupied.

Peiper\* and Rumpf† have shown diminished alkalescence of the blood to be of common occurrence apart from gout. More recently an acid reaction of the blood has been shown to occur occasionally; this points to the necessity of a reconsideration of the accepted axiom that blood is always alkaline, and of a fresh study of the blood in gout from this special point of view.

#### THE ALKALINE TREATMENT.

Ancient pharmacology has to be scrutinized rather closely for any evidence of the use of alkalies and alkaline earths in gout. They seem to have played a subordinate part until the middle of the last century. The ashes of various plants prescribed in antiquity were probably not credited with greater virtues than a thousand and one useless remedies then in vogue. Nevertheless, even in those early days, whether as the result of observation or merely as a happy guess, reference was made by some authorities to the beneficial action of earths or alkalies in calculous disease. Pliny recorded a belief that the shells of snails would expel stone; Vitruvius mentions mineral waters possessing a solvent power over stone in the bladder; and Galen refers to the power of splitting up renal calculi attributed to the concretions within the sponge. A curious allusion by Paulus Ægineta to certain authors deprecating the unskilled use of solvent remedies, 'lest they should lead to an increase in the size of the stone,' reminds us of similar reservations applicable at

<sup>\*</sup> Virchow's Archiv, 1889.

<sup>†</sup> Centralblatt f. Klin. Med., 1891.

the present time to the use of some of the alkaline earths.

The caution against the misuse of these remedies implied a belief in their power. Robert Boyle was, according to Lecorché, whose work supplies these historical references, one of the earliest representatives of the idea of the chemical solution of stone in the bladder by internal remedies, and Boerhaave explained the solvent action of alkalies by assuming that the concretions were bound together by some acid which an alkali would remove.

The treatment of gout in Germany by the administration of vegetable ashes in Rhine wine was a revival of the 'decoction of ashes' of the ancients, and in this country Miss Stephens' remedy—containing among its ingredients eggshells and soap—was a distant imitation of the remedy mentioned by Pliny. Its prolonged use was thought by Huxham to be productive of harm.

Sydenham, who recognised the diuretic action of the lixiviating salts in dropsy, did not insist on their value in gout. It was reserved for Cullen to dwell upon the practical use of the salts of lime, of the absorbent earths, and of soap in the treatment of tophi. Whytt's 'Essay on Lime-water,' Edinburgh, 1752, should also be mentioned.

The demonstration of the presence of uric acid in tophi by Tennant and Pearson, by Wollaston, and by Fourcroy at the close of the eighteenth century, established the reputation of the alkaline treatment on a chemical basis, and since then it has received increasing recognition. Scudamore and Barthez recommended the alkaline and the ammoniacal carbonates; Galtier Boissière insisted on the special value of the potassium salts; Ure\* called

<sup>\*</sup> Lond. Med. Gazette, November, 1844; and Med. Times and Gazette, vol. ii., 1845, p. 145.

attention to the properties of the salts of lithium; and Buckle, of Baltimore,\* advocated the use of ammonium phosphate.

In some quarters, however, the new method met with strenuous opposition. Trousseau brought against it the charge of converting acute sthenic gout into the chronic ailment, and of setting up the symptoms of the alkaline cachexia, viz., debility with anæmia, and tendency to hæmorrhage. Owen Rees and Golding Bird were also numbered among its opponents. To what extent these objections may have been well founded we shall presently consider. They did not suffice to stem the tide, and the chemical arguments put forward by Garrod gave strong additional support to this method, which became, as it were, the classical method of treatment, although in practice its application was by no means always rigidly enforced, and of late years has been varied by the introduction of entirely new medicinal agents.

Trousseau's adverse criticism had been made from a purely clinical standpoint.

After a long interval a more serious objection has now been raised by Sir W. Roberts from the chemical aspect of the question. This we shall proceed to set forth after stating the case as originally made out in favour of the method.

#### THE RATIONALE OF THE ALKALINE TREATMENT.

The Solvent Action of Alkalies.—The explanation first suggested, and long accepted without any question, was based upon elementary chemical considerations in connection with Wollaston's discovery of the uratic composition of tophi, and with Garrod's discovery fifty years

<sup>\*</sup> Cf. Med. Chir. Review, 1847.

later of the presence in the blood in gout of an excess of uric acid. The alkaline urates being much more soluble than uric acid itself, it was argued, not without much apparent reason, that the administrations of alkalies would cause the gouty concretions to be dissolved. Although this result did not always follow with the completeness which might have been anticipated, the theoretical correctness of the doctrine remained unchallenged, and it was also supported by the following considerations.

The neutralizing action of alkalies was regarded as a safe means of obviating the formation of uratic concretions. Not only was the acidity of the uric acid itself disposed of, but the excessive acidity which was a well-ascertained feature of gout, and to which the precipitation of uric acid was rightly attributed, was also to be suppressed by the alkaline dose. The fact that the intensely acid gouty urine was rendered alkaline was held to be a demonstration of the fulfilment of the indication.

Sir W. Roberts' investigations have robbed this argument of its force. The reaction of the urine cannot be taken as an accurate measure of the relative condition of the blood.

The Reaction of the Blood.\*—The question as to the varying alkalinity of the blood had already been touched upon by Sir A. Garrod, who had never found acidity, but at most reduced alkalinity, in the blood serum in gout. Sir W. Roberts considers that the reaction may at most verge on neutrality. A diminished alkalescence of the blood is not special to gout; it has been described in connection with the various forms of cachexia, anæmia, leucocythæmia, acute rheumatism, pneumonia, diabetes and pyrexia.

Sir W. Roberts points out, in connection with the same

subject, that it is difficult to disentangle the question of the possible influence of the complications of gout on the constitution of the blood from that of the direct effect of pure gout; and, in order to avoid any confusion, the field of study would have to be restricted very carefully to the latter.

There are, of course, other aspects to the administration of alkalies in gout besides that of an attempted solution of the deposits, and this does not escape Sir W. Roberts' attention. Among the reasons often given for their administration is the alleged undue prevalence of acid in the gouty system; and this, as stated by Sir W. Roberts, is sometimes regarded as amounting to a dyscrasia.

The Insolubility of the Sodium Biurate.—The common belief that the alkaline carbonates and phosphates, by increasing the alkalescence of the blood, add to its solvent power on gouty deposits, and delay or prevent their formation, is negatived by Sir W. Roberts' experimental evidence. He has clearly proved that alkalescence, as such, has no effect whatever on the solubility of sodium biurate; and he has shown, moreover, that the addition of an alkaline carbonate to blood serum impregnated with uric acid produces no appreciable effect on the process of maturation, and on the advent of precipitation of the crystalline biurate.

In this respect the medicinal treatment of gout and that of gravel are shown by him to stand on an absolutely different footing. 'The urine is a dead excretion' without power of self-purification, whilst 'the blood is a living stream with high powers of self-adjustment to a normal standard.' Again, 'whilst the daily average of urine discharged amounts to some 50 oz., in gout we are seeking to make an impression on a much larger bulk

of fluid, viz., on the totality of the blood, lymph, and synovia, a quantity, in a man of average weight, certainly not less than 20 lb. A practicable dose of alkaline carbonate which will enable us radically to alter the urine will produce little impression on the larger bulk of fluid, since any surplus alkali will be expelled with all speed through the kidneys. However valuable, therefore, the administration of alkalies may be in the treatment of gravel, Sir W. Roberts does not find any direct object in their administration for gout.

The Clinical Failure of the Alkaline Plan. — Sir W. Roberts supplements this chemical criticism by conclusions derived from clinical observation: 'I have repeatedly administered the bicarbonate and citrate of potash continuously for three or four years, and in sufficient doses to maintain the urine persistently alkaline, yet I have seen the arthritic attacks recur with unabated regularity.' This experience is probably that of many practitioners, though few may have given the remedy so patient a trial.

The alkaline cachexia dreaded by Trousseau is not mentioned among the disappointments incidental to this prolonged alkalization of the urine. We are also reassured as to the probability of so untoward a result by a consideration of the large doses of alkali which can be ingested and passed through the kidney without any material alteration taking place in the reaction of the blood.\*

At the same time, where potassium salts are employed, we should not lose sight of the toxic properties of the metal, which are dwelt upon under another heading. Chronic gout is essentially a debilitating disease, and in the course of its treatment, which cannot altogether re-

move the debility, any drug bearing an evil name as a depressant is sure to be charged with some of the blame. The advisability of avoiding the use of depressing therapeutic agents will be insisted on in connection with the treatment of chronic gout.

The alkalies have thus failed to fully justify their original reputation for efficiency. They fulfil imperfectly the two chemical indications for which they were intended. The solution and reabsorption of tophi is not to be brought about by any but the stronger solutions of potassium salts, and a powerful alkalization of the blood is not so easily to be obtained. From their failure in these directions, it by no means follows that the alkaline method is useless, or that the individual alkaline remedies are inert in gout, unless pushed to their toxic doses; but the farther we step away from mere chemical reactions and formulæ, the more difficult it becomes to provide scientific evidence of their value. Nevertheless, long accumulated clinical evidence, and the constantly recurring testimony of patients under treatment, must carry weight in considering the practical question.

Whether, as has sometimes been alleged, the kidneys may be assisted by alkalies in the act of separating uric acid from the blood is matter for pure speculation. There is no obvious improbability in this, and much to suggest it as likely; but experimental evidence is still wanting, and the present data are of a somewhat contradictory nature.

Physiology provides us, however, with suggestions of a more definite kind in connection with metabolism, and particularly with hepatic metabolism. Two theories have been entertained in explanation of the beneficial results undoubtedly obtained by the administration of some of the alkalies or alkaline earths, and to these we may refer

under the heading of the alterative and oxidation theory, and the theory of hepatic and glandular stimulation.

The alterative action of alkalies and of their salts is hitherto imperfectly understood. It probably depends largely upon their solubility, which brings them into intimate contact with all the constituents of the body; any affinities which they may possess are in this way brought extensively into play. The powerful attraction of the alkaline metals for oxygen, and of their hydrates for water, sufficiently explains their destructive caustic action on tissues. Their salts are destitute of any strong action of this kind. A distinction must be made, however, between the alkaline salts of the mineral acids and those of the organic acids, and especially of carbonic acid. The relatively feeble stability of the combinations belonging to the latter group brings them perceptibly nearer to the hydrates in their physiological action. The alkaline carbonates are more likely to be split up and to yield a supply of the base available for combination with the tissue elements. For the latter the alkalies and especially potash, possess a marked affinity, which is probably not limited to the formation of alkali albuminate with their albumen.

In these various ways the alkaline salts bring about an appreciable increase in the rate or in the activity of metabolism. If they do not themselves play the part of oxidizers, they promote in the tissues changes which are bound up with oxidation. An indirect proof of the accelerated metabolism is afforded by the increased excretion by the kidney of urea and of sulphuric acid noted by Parkes after small doses of liquor potassæ, and by the fact that 'an increased consumption of sodium chloride not only increases the quantity of it and of urea in the urine, but also increases the excretion of potash

salts; whilst, on the other hand, potash salts also increase the excretion of sodium.'\*

It is superfluous to point out that the torpid metabolism of gout is a special indication for the employment of agents of this kind.

The stimulating effect on the mucous membranes and their glands is another important recommendation. Much of the benefit is doubtless to be ascribed to the solvent action for mucus, and in the intestinal canal to the local neutralization of any excess of acidity. In addition, they increase the amount of gastric juice and the flow of bile. Clinical evidence of their value in dyspepsia has been abundantly corroborated by physiological experiments.

Their diuretic action, combined with their antacid property, is also of direct service in promoting elimination of the soluble excreta.

This brief review of some of the physiological activities of the alkaline salts will suffice to show that their usefulness in gout cannot be correctly measured by their coefficient of solvent power for uratic deposits, nor even by the increase of alkalinity which they may confer on the blood. We shall now proceed to note the individual peculiarities of each member of the group.

<sup>\*</sup> Lauder Brunton, 'A Text-book of Pharmacology, Therapeutics, and Materia Medica,' p. 527. London: Macmillan and Co., 1885.

#### CHAPTER XLII.

# THE ALKALINE SALTS AND THEIR USES IN GOUT.

#### THE SALTS OF POTASSIUM.

Lecorché attributes to J. Guérin (1746) the earliest published observations of the efficacy of potassium salts in uric acid gravel, and to Mascagni (1804) a confirmation of the same favourable report; whilst Rendu claims for Galtier-Boissière the honour of that discovery. The solvent power of potassium salts has been amply proved since then, and they have been freely used in this country, and subsequently on the Continent. They had, however, been administered for gout by the ancients in the vegetable ashes then prescribed.

Garrod's experimental demonstration of the rapid solution of uratic deposits in cartilages immersed in a solution of potassium carbonate, whilst sodium carbonate solutions exerted hardly any solvent action, have been confirmed by Sir W. Roberts, who has shown that, in their marked influence in delaying the maturation of the sodium biurate, the potassium salts occupy, in the alkaline group, a unique position. They are, from the point of view of the uratic precipitations in gout, the remedies par excellence. Moreover, their alkalizing power exceeds that of the other alkalies, with the exception of lithium. Their diuretic action is also greater than that of any of the others.

The physiological affinities of potassium are also quite special. Potassium, in combination with phosphoric acid,

is a constituent of all growing cells, and is largely contained in the red blood-corpuscles—which hold it firmly, in spite of its high solubility and of the facilities for its escape into the plasma—and in the substance of muscles. In connection with this strong attraction exerted on them by the solid elements of the tissues, the salts of potassium are credited with a stronger metabolic influence than those of sodium and of lithium. This may also be correlated with the toxic action special to them. According to Rendu, 6 to 8 grammes will act as a poison, whereas much larger doses of sodium are harmless.

The toxicity of the salts of potassium has been studied by Feltz and Ritter, and subsequently by Bouchard,\* in connection with the toxicity of urine, and with the pathogenesis of uræmia.

Bouchard states that the quantity of sodium chloride which would kill I kilogramme of animal is 5'17 grammes, and this is the most toxic of the salts of sodium. Thus, the total amount secreted in twenty-four hours would only kill 2 kilogrammes, whilst the total urine itself would kill 30 kilogrammes. The most toxic among the salts of potassium-viz., the chloride-kills in the proportion of 18 centigrammes per kilogramme of animal; the phosphate is not toxic under a proportion of 26 centigrammes, and the phenylsulphate is still less toxic. In spite of the high toxicity of the salts of potassium, Bouchard cannot agree with the conclusions formed by Feltz and Ritter, to the effect that the toxicity of urine is due to its mineral constituents. In order to kill by potash, a quantity is sometimes needed double that which is contained in the quantity of urine (40 to 60 cubic centimetres, or on the average 45 cubic centimetres) which usually causes death. Moreover, whilst death from potash is preceded by convulsions, this is not the case with poisoning by normal urine secreted in

<sup>\*</sup> Cf. 'Auto-intoxication in Disease,' p. 120 et seq.

the middle of the day; neither is arrest of the heart noticed in this case. From the fact that healthy decolourized urine kills without convulsions, Bouchard supposes that an antagonism may exist between potash and the 'convulsive urinary principles.'\* On the other hand, some pathological urines, especially the febrile, retain their convulsive power in spite of decolourization; this, Bouchard suggests, may be due to an excess of potash derived from an increased cellular destruction.

Moreover, Bouchard's experiments show that the charcoal filter, which retains only one-sixteenth of the total potash, removes one-third of the toxicity of urine (colouring matter, extractives, and alkaloids), including a convulsive, a pupil-contracting, and a temperature-lowering principle.

At the most, Bouchard estimates the 'mineral' toxicity of urine at 57 per cent. of the total urinary toxicity, and the 'potassium' toxicity only at 47 per cent. of the same.

The following table of toxicity, drawn up from experiments by Bouchard and Tapret, but which unfortunately does not include lithium, illustrates the strong contrast between the salts of potassium and those of sodium. The weights in grammes represent the quantity of each substance which is necessary to kill one kilogramme of animal:

		Index of Solution.	Grammes.
Chloride of potassium	-	- 1180	0.180
Sulphate of potassium	-	- 200	0.181
Phosphate of potassium	-	- 200	0.263
Chloride of sodium	-	- 10	5.12
Sulphate of sodium	-	- 10	9.00
Phosphate of sodium	-	- 10	6.00
Chloride of magnesium	-	- 200	0.463
Sulphate of magnesium	-	- 200	0.245
Chloride of calcium	-	- 200 0	1.011

<sup>\*</sup> These Bouchard has shown to be insoluble in alcohol, their antagonists, the narcotic urinary principles, being soluble.

These observations are worthy of consideration in connection with gout, in which it is known that the elimination of the urinary constituents is not at all times performed with completeness.

Death in potassium-poisoning is due to arrest of the heart's action, and is preceded by convulsions. The action is supposed to be a direct one on the tissues, and particularly on the nervous, muscular, and cardiac tissues. In the language of therapeutics, potassium salts are depressants, and this is an important, though it appears to be the only, reservation to be made in connection with its use. As a diuretic and solvent, as an alkalizer, as a diaphoretic, as an hæmatinic, and in the accelerating influence which it exerts on metabolism, it is a powerful and beneficial agent.

The usual form for its administration is the bicarbonate, of which small doses are harmless, and larger doses, such as a drachm, are often in other diseases, and particularly rheumatism, continued for many days without any evil effect.

#### THE SALTS OF SODIUM.

The peculiarities of the sodic salts are the converse. They are free from the reproach of toxicity in the ordinary range of their administration, but they incur that of inefficiency as solvents of uric acid—nay, the graver reproach of promoting its precipitation—and to this we shall presently revert.

Beneke,\* in contrasting the potassium and sodium compounds, refers to the diverging mode of chemical reactions observed by Kolbe,† who obtained salicylate of sodium from sodium phenate and carbon dioxide, whilst potassium phenate yields the paraoxybenzoate—

<sup>\*</sup> Journ. für Prakt. Chemie, 1874. † Quoted by Lecorché.

and he regards the physiological actions as different also, sodium salts taking effect chiefly on the fluids and determining a temporary alkalinity, whilst the potassium salts tend to combine with the tissues.

The physiological affinities of sodium are also the converse of those of potassium. It does not enter so largely into the constitution of the solid elements, but is tenaciously held by the serum and other fluids. A minimum supply of sodium chlorides is well known to be one of the most urgent necessities of the organism, whilst an excess of this commodity is well borne, and does not raise the sodic standard of the serum, but passes out harmlessly through the kidneys.

These remarkable facts dispose in great measure of the objection urged by Trousseau and others against the free use of this alkali. Rendu refers to the results of Charcot and Bouchard, who administered as much as 30 grammes of the bicarbonate daily for months without producing any anæmia; and he does not conceive that the alkaline cachexia can be set up by anything short of a long continuance of enormous doses of the salt.

On the other hand, the persistence, for prolonged periods, of an alkaline reaction after the temporary use of moderate doses of the alkaline salts is not so easily explained in the case of the sodium bicarbonate as in that of the salt of potassium, and we see in it an indication of a definite alterative action special to sodium.

The insolubility of sodium urate has always been urged against the medicinal use of the sodic salts; and in connection with the every-day treatment of gout, and with its treatment by mineral waters, this objection has taken a practical form, and has given rise to discussions which will be considered in another section. It will be readily perceived, however, that too much might be made of

the allegation in question. The ordinary gouty person is never sodium-starved. There is always present in his economy a considerable excess of sodium over and above the indispensable minimum, an excess much larger than the quantity which might be claimed for the disposal of the daily accumulation of uric acid in the shape of biurate. It does not appear that any additional excess could affect the result. This is a uric acid question, not a sodium question. If it could be shown that undue richness of the blood in sodium led to an increased formation of uric acid, we should indeed be careful in its administration. On this point experimental evidence would be welcome; it must be owned that hitherto clinical evidence inclines in the opposite direction. Lecorché does not hesitate to ascribe to sodic salts a power of diminishing the formation as well as that of promoting the excretion of uric acid.

The action on the mucous membrane mentioned as one of the properties of alkalies is conspicuously possessed by the sodium bicarbonate, which is almost universally prescribed in preference to any other salts for the relief of dyspepsia. This success is partly due to its direct stimulating effect on the gastric secretion, but there is another property which it does not share with any other metal, and which largely explains its many-sided usefulness.

As a cholagogue and hepatic stimulant sodium possesses an undisputed advantage over potassium and other members of the group. It is an essential constituent of bile, as the combining base for glycocholic and taurocholic acid, and the ingestion of its salts has been proved by repeated experiments to promote the flow of bile. A dose of Vichy water leads to an immediate discharge of bile in dogs presenting a biliary fistula. To this chola-

gogue action much of the therapeutic value of sodium bicarbonate is doubtless to be ascribed. By stimulating the function of the liver, it must efficiently assist in restoring the mucous membranes to a healthy condition. Catarrhs in general, not only those of the stomach, intestines, and biliary ducts, but also the genito-urinary and bronchial catarrhs, are much benefited by its administration in aërated solutions.

These advantages make out a strong case in favour of the sodium treatment. Lecorché gives it his decided support. Having observed a persistence of the alkaline effect of sodium salts for a considerable time after a few days' administration, and bearing in mind the cardiac depression, the occasional diarrhœa, and other risks attaching to medication by salts of potash, he strongly prefers the sodium compounds to all others, including those of lithium; and he regards them as not markedly inferior in the three actions which he attributes to alkalies, viz., (1) that of checking undue dissociation of organic cells; (2) that of dissolving deposits of a uratic nature; (3) that of opposing an increased alkalinity of the blood to the tendency to precipitation of the acid biurate. Thereby the out-put of uric acid is much increased.

At the same time, the most sanguine advocate should not overlook the question of individual peculiarities in the patient. Some persons are much more readily alkalized, and others stand alkalizing very badly. Judgment should be exercised in discriminating cases.

Again, any remedy may be administered too freely, too continuously, or too long. The question of doses is an important but difficult one. Effects very dissimilar, and even contrary, may sometimes be obtained from the same agents, according as they are used in minute or in excessive

amounts. A comparative study of this kind is needed in the case of the sodium salts in connection with the treatment of gout, by reason of the wide range of their nontoxic dose. For the present, we should be content with the decided benefit accruing from their administration in moderate quantities so long as we lack evidence of their mode of action when given on a larger scale.

Their intermittent employment is also to be preferred to their continuous administration through prolonged periods. The indications for an interruption of the treatment will be supplied by the peculiarities of each case. They probably form no exception to the rule that the activity of drugs is lessened by the establishment of 'tolerance,' and that the advantage which may thus be lost is to be measured by the degree of their initial efficacy.

In conclusion, the strongest proof which we can adduce of the value of the sodium salts in gout is the fact that to the present day they are largely prescribed, especially on the Continent, and largely taken also in the shape of mineral waters, in spite of the experimental evidence which has denied to them any important direct solvent power for uratic deposits, and placed them under a suspicion of increasing their precipitation. They have, moreover, enjoyed a much earlier popularity in connection with gout than those of potassium, and especially of lithium, the last-named having been introduced at a comparatively recent date; for sodium is stated to have been the basis of Sydenham's 'lixiviating salts,' and of the soaps recommended by Van Swieten, Cullen, Boerhaave, and many others.

## THE SALTS OF LITHIUM.

The question as to the value of lithium in gout has given rise to considerable discussion, and is still sub judice.

Discovered by Arfewdson in 1817, in petalite, it has since then been obtained from lepidolite, and from numerous mineral springs, including those of Carlsbad, Aix-la-Chapelle, Marienbad, Kissingen, Ems, Teplitz, Bilin, Kreuznach, Vichy, Baden, and many others; it has, moreover, as stated by Garrod, been recognised by means of the spectroscope as one of the most widely diffused metals throughout the vegetable and the animal kingdom, and 'must be regarded, not as a drug foreign to the economy, but as a normal constituent of the body.'

The solubility of uric acid in solutions of carbonate of lithium was first turned to a therapeutical purpose by A. Ure, who proposed to inject the carbonate into the bladder as a solvent for stone, and described, in the Pharmaceutical Journal for 1843, his experimental trial on a stone immersed into a solution kept at the temperature of the body. Sir A. Garrod was, however, the first to employ the remedy systematically for the treatment of gravel and of gout. Adding a further proof of the extraordinary solubility of the lithium urate to that given by Lipowitz, who found that uric acid, when boiled with pulverized lepidolite, displaces the silicic acid of the mineral in virtue of its more powerful affinity for lithium, he showed that, 'when carbonate of lithia in excess is boiled with water, the addition of uric acid causes it to dissolve, proving that the urate of the base is more soluble than the carbonate,' and identified the long crystalline needles subsequently obtained as those of the biurate of lithium.

By placing pieces of cartilage infiltrated with uratic deposit into saline solutions of the three metals, he found that after forty-eight hours the lithia had completely dissolved the incrustations, potash only part of them, and soda not any.

These and similar experiments placed beyond doubt the

solvent power of the metal for uric acid even when embedded in the tissues, and led him, in 1858, to administer the carbonate of lithium internally.

The chemical properties of lithium are those of an alkaline metal. In specific gravity and in atomic weight, it is the lightest of metals. Under equal weights, its salts therefore represent a higher neutralizing power than those of sodium or potassium. The carbonate is less soluble (I in 150 of water) than the sodium and also than the potassium carbonate, but an excess of carbonic acid improves its solubility. The citrate is much more soluble (I in  $2\frac{1}{2}$  of water).

Its action in the economy has been regarded as that of an alkalizer of the blood and of the urine, of a solvent for uric acid, and of a diuretic.

Its physiological and toxic effects closely resemble, but are supposed to exceed, those of potassium. It is a depressant to the tissues, particularly to those of the heart and nervous system. This circumstance accounts for its relatively small therapeutic dose. The carbonate taken in larger quantity than 45 grains a day was found by Charcot to set up dyspepsia. Various nervous symptoms have from time to time been observed during its administration. Garrod mentions slight tremor in one hand in two cases with unsound kidneys, and twitchings in both arms in another patient taking very large doses.

The therapeutical results obtained by Garrod included, besides diuresis and alkalization of the urine, with disappearance of gravel, a marked immunity from the recurrence of gouty attacks, and, as reported by the patient, a reabsorption of gouty concretions. It should be borne in mind that the mode of administration in considerable dilution, which has been adopted at Garrod's original suggestion, is in itself a remedial measure.

Whilst confirming Garrod's observations as to the immediate diminution in the amount of uric acid excreted, Lecorché\* is unable to corroborate his statement as to the strong diuretic and alkalizing effect of lithium salts. In neither of the two cases of which an accurate observation was made was there any permanent diuresis; in one of them even temporary diuresis failed to occur. Daily doses of 15 and of 30 grains of the carbonate, whilst depressing the acidity, did not produce an alkaline reaction of the urine. He also finds that urea and phosphoric acid are markedly diminished in the urine, as well as the uric acid. The alkaline bases (potassium and sodium) are also diminished, but more particularly calcium and magnesium.

Sir W. Roberts states, in connection with lithium carbonate and piperazin, that 'they do not confer upon blood serum or synovia (when added to them in o'r per cent. to o'r per cent. solutions) the slightest help in dissolving sodium biurate, nor in retarding its precipitation. Their beneficial effect, if it exists, is not to be traced to their solvent power on sodium biurate.'

These discrepancies called for a renewed investigation of the pharmacology of lithium. The same need is yet more strongly indicated by the recent criticism of Dr. Haig,† who also finds that lithia diminishes the excretion of uric acid. This is in apparent contradiction with Sir A. Garrod's opinion that urate of lithium is one of the most soluble of the urates, and Haig suggests an explanation. He states that lithia given by the mouth is of no use as a solvent for uric acid, because, as shown by Rose,‡ it forms a nearly insoluble triple phosphate with phosphate of sodium, or with the triple phosphates of ammonium

<sup>\*</sup> Loc. cit., p. 557 et seq. + Loc. cit., pp. 29, 30. ‡ 'Chemical Analysis,' p. 15.

and sodium, salts which are generally present in animal fluids. Even if this were to receive a further experimental confirmation, it would not prove conclusively that the salts of lithium are inert. We possess abundant evidence that some of the most insoluble substances undergo partial solution in the organism. A fortiori might this result be expected in the case of a body many of the combinations of which, and in particular the urate, are extremely soluble. On the other hand, this would go far to explain the diverging estimates which have been formed of its specific utility in gout. Taken in conjunction with the fact that, in spite of the experimental demonstration of the unequalled solubility of lithium urate, upon which such fair hopes had been founded, lithium has not secured, after a prolonged trial, a leading position in the treatment of gout, the suspicion which has been thrown upon the genuineness of its most valuable medicinal property leaves us in an attitude of reserve. We are bound to take heed of the relative failures which have been reported by various clinical observers; but we cannot lose sight of the favourable testimony supplied by others and by the patients themselves.

The question is whether these salts may not be capable of very different activities under varying circumstances and in different subjects. On the other hand, the limitations due to their toxicity make it probable that we have already gauged the range of their usefulness.

## THE SALTS OF AMMONIUM.

Ammonia and its salts enjoyed among the ancients a reputation which has not been maintained. The disuse into which they have lapsed is partly due to the acknowledged superiority of the salts of the fixed alkalies. It is

justified on chemical grounds by the circumstance that ammonia is not excreted as an alkali, but as nitric acid. It increases the acidity of the urine, and cannot, therefore, be regarded as a solvent of gravel. Sir W. Roberts has shown that its salts do not possess solvent power for the biurate of sodium, but rather check its solubility in more favourable media to which they may have been added. His results are at variance with the statements formerly made by Garrod, that ammonium phosphate possesses considerable solvent power for sodium biurate.

Buckler,\* to whom a revival of the ammoniacal treatment was due, thought that he had retarded in thirteen patients, by the administration of ammonium phosphate, a return of the gouty attack, and that he had also taken some effect on the concretions. S. Edwards† also advocated its use, on the ground that the neutral phosphate would give rise to a soluble ammonium urate, and recommended that from 120 to 150 grains should be given each day.

Sir A. Garrod declared himself well satisfied with the results obtained from this salt in cases of chronic gout.

Although we cannot now attribute a specific value in gout to any of the ammoniacal salts, their general properties are eminently serviceable in the treatment of the various ailments of gouty patients. As stimulants, as diaphoretics, and as diuretics, they will be found useful.

The ammonium chloride deserves special mention as an important hepatic stimulant and cholagogue, and also as a valuable remedy in some forms of neuralgia to which the gouty are liable. In these various capacities it will probably receive more attention in connection with gout

<sup>\*</sup> Amer. Jour. of Med. Sc., January, 1846, quoted by Lecorché.

<sup>†</sup> Lond. Med. Gaz., June, 1850, quoted by Lecorché.

than has hitherto been awarded to it. In common with, but in a higher degree than, the other salts of ammonium, it is credited with the power of increasing the output of urea and of uric acid. Ammonia itself has been suspected of entering into the formation of these bodies.

## THE SALTS OF CALCIUM AND OF MAGNESIUM.

It will not be necessary to dwell long on the therapeutic action of these substances in gout. Their great reputation was anterior to the full appreciation of the stronger claims of the alkaline salts; but they have preserved an important place in practice, and are to the present day largely used, and with considerable benefit, although we cannot boast of any accurate knowledge of their mode of action.

The chemical properties of the two sets of salts present many points of resemblance with well-marked differences, especially as regards their solubility.

The physiological actions differ widely, calcium salts being astringent, and magnesium salts purgative. In some respects they agree. Reference to Bouchard's table of toxicity\* will show that in their toxic equivalent they are not far apart, magnesium being twice as poisonous as calcium, though much more likely to be quickly eliminated; and that they approach much more closely the potassium salts than the salts of sodium.

Of their intimate actions on the tissues we know nothing. Lauder Brunton+ and Cash have shown that calcium does not regularly increase the contractile power of muscle, but, like sodium, increases the duration of the contraction, and the muscular viscosity or contracture · the latter is enormously increased by barium; whilst

<sup>\*</sup> Cf. p. 378.

potash diminishes both. On the vessels calcium, magnesium and barium produce contraction, though in much less a degree than potassium chloride. On the excised heart of the frog artificially fed by saline solution, the addition of minute quantities of chloride of calcium prolongs the contractions, which can be restored to their normal length by a trace of potash, without any of the weakening effects being then induced which are special to the latter.

The therapeutic virtues common to both in gout are, so far as known, chiefly their antacid and diuretic properties. Calcium is chiefly excreted by the bowel; so is magnesium when it purges, but in non-purgative doses it passes out through the kidneys, acting as a diuretic as well as an antacid. The diuretic action of calcium is largely due to the copious dilutions in which it is usually administered in gout.

The salts of calcium have undoubtedly been used with good results in gout. In reviewing this subject, Lecorché accepts Lieutaud and Morand's experimental conclusions to the effect that Miss Stephens' remedy (soap and eggshells) owed its efficacy to bicarbonate of lime. Subsequent experiments were conducted by Holly, who arrived at the same conclusion. Later Whytt succeeded in curing the gravel by the administration of one to two pints of lime-water, continued daily. The same treatment prevented the return of the gout in a patient who had suffered from severe and recurrent attacks. Lecorché also refers to Gilbert Blanc's observation of a lengthening of the intervals during its use.

The beneficial effects of calcareous mineral waters, such as those of Contrexéville, Vittel, Capvern, Pougues, etc., which contain chiefly lime, are too well attested to admit of doubt. In presence of the fact that urate of calcium

is highly insoluble, it is difficult to explain them on the lines of the uratic theory of gout. We shall return to their consideration when discussing the uses of mineral waters. We should not lose sight of the sedative action of weak solutions of lime on the alimentary mucous membrane, and of their solvent power for mucus, in addition to the antacid and diuretic properties which we have dwelt upon.

The salts of magnesium probably possess greater value than the prevailing plethora of minor remedies for gout gives us a chance of realizing. On this point earlier observations might be consulted with advantage. Brande\* narrates how a patient whose gastric symptoms had led to the use of magnesia ceased to observe uric acid in the urine, and remained free from gout for a longer period than during any of the six previous years. Scudamore also believed in the efficacy of magnesia or of magnesium carbonate, although he objected to the constant daily 'employment of alkalies on the simple principle of preventing gout.'

Few gouty patients at the present day have never experienced in some form or other the benefit of this medication. The black draught and the white mixture seldom fail to relieve, and their magnesian constituents and the milder citrate form the basis of various aperient salts largely used under different names. Again, many laxative mineral waters, such as those of Carlsbad and of Marienbad, are largely indebted to magnesium for their efficacy in gout.

We are as ignorant of the nature of any intimate influence which may be exerted by these salts on the tissues as in the case of those of calcium. The obvious

<sup>\*</sup> Edinburgh Med. Phys. Essays, iii., p. 450, quoted by Lecorché.

results are traceable to their combined purgative, antacid and diuretic properties. Magnesia itself and its carbonates exercise in addition a powerful check upon the acidity of the stomach, and in some cases of gouty dyspepsia and gastralgia they are sovereign remedies.

### SOME RECENT ALKALIZING REMEDIES.

The chief representatives of this group of powerful organic alkalies are piperazin, lysidin, and lycetol. In virtue of their extraordinary neutralizing power for acids, great results were expected of their administration in gout. These hopes have not been realized. Favourable accounts\* of their employment are hitherto too few to establish their reputation.

Lysidin,+

possessing five times the alkalizing and the uric acid solvent power of piperazin, is a hygroscopic, reddish-white soluble powder, the taste of which is said to recall the smell of mice. It is obtained as a hydrochlorate by the dry distillation of ethylene-diamine-hydrochlorate with sodium acetate. Its much greater strength as a solvent renders any further reference to the weaker solvent piperazin unnecessary.

E. Grawitz, t who administered in increasing doses from I to 5 grammes of lysidin daily to two patients with

<sup>\*</sup> Cf. Heermann (Therap. Monatsch., 1894, viii., p. 561), Mapother (Practitioner, 1894, p. 265), and Biesenthal (Virch. 'Arch.,' 1894, exxxvii., p. 31)—quoted in the Year-Book of Treatment, 1895, pp. 126, 127—speak favourably of piperazin.

<sup>†</sup> These data are supplied by Dr. A. Garrod in the Year-Book of Treatment for 1896.

<sup>‡</sup> Deutsch. Med. Wochensch., 1894, xx., p. 786.

tophaceous gout, reports definite results, such as a marked diminution of the tophi on the epiglottis and in the neighbourhood of the joints, and a marked improvement in the mobility of the joints. But, in common with other observers, he failed to obtain any evidence of an increase or of a diminution in the excretion of uric acid, and he was driven to the conclusion that a portion only, if any, of the uric acid from the tophi was excreted by the kidneys as such.

G. Klemperer and A. von Zeisig\* treated three typical cases of gout with lysidin, but were unable to trace any influence on the symptoms, or on the excretion of uric acid.

Sir W. Roberts had demonstrated the failure of piperazin to assist blood serum or synovia in dissolving sodium biurate or in delaying its precipitation. Martin Mendelsohn,† to whom we owe the observation that the uric acid solvent power of piperazin and of lysidin is abolished by the smallest admixture of urine owing to the sodium chloride it contains, is of opinion that gouty tophi may perhaps be dissolved by these agents, and states that uric acid is dissolved by them in serum nearly as well as in water. This view does not appear to be compatible with Sir W. Roberts' statement concerning piperazin. At any rate, they are obviously powerless to effect the solution of any concretions within the urinary tract.

Lycetol (dimethyl-piperazin-tartrate) has been well spoken of by Wittzach,‡ who obtained good results in a case of gout. It is stated to be equal in power to piperazin, not hygroscopic, and pleasant to the taste.

<sup>\*</sup> Zeitsch. f. Klin. Med., 1895, xxvii., p. 558.

<sup>+</sup> Deutsch. Med. Wochensch., 1895, xxi., p. 283.

<sup>‡</sup> Allg. Med. Cent. Zg., 1894, No. 7; and Therap. Monatssch., 1895, p. 387.

Uricedin is said to be a mixture of salts (the citrate, chloride, and sulphate of sodium, and the citrate of lithium). Meisels reports that it does not display the power possessed by piperazin of preventing the deposition of urates in the tissues of birds after the subcutaneous injection of potassium chromate. In man, far from increasing, it rather diminishes the excretion of uric acid. It does not appear, according to his observations, to be entitled to a place among the solvents for uric acid.

## CHAPTER XLIII.

# THE SALICYLATES AND OTHER REMEDIES IN GOUT.

## SODIUM SALICYLATE AND THE SALICYLIC GROUP.

The uncertainty which still prevails as to the value of these substances in gout is shown by the fact that some recent writers on pharmacology do not mention gout among the affections for which they are of use, and others even describe them as useless. On the other hand, among writers on gout they have found some strenuous supporters.

The members of this group to which we should devote attention are the salicylates of sodium, of quinine and of lithium, salicin, and saligenin.

Salicylic acid (HC<sub>7</sub>H<sub>5</sub>O<sub>3</sub>), obtained from the salicylates contained in the oils of wintergreen and of sweet birch, is also artificially prepared by combining carbonic acid gas with carbolic acid, a much less trustworthy source. Its salts only are employed in gout.

Salicin (C<sub>13</sub>H<sub>18</sub>O<sub>7</sub>), a glucoside obtained from the bark of the willow and of the poplar, is not largely used, its action being less powerful, though it is said to be better sustained and less depressing to the heart and vascular system.

Saligenin (C7H8O2) is produced from salicin by the

separation of glucose. It has been recently tried by Walter,\* who reports good results from its use.

The salicylates of quinine and of lithium are usually administered in doses too small to bring the salicylic radical into action, though they may do good service through their basic constituent.

Sodium salicylate, the preparation almost invariably prescribed, behaves in the same way as salicylic acid, part of which combines in the blood or in the tissues with glycocine to form salicyluric acid—

$$HC_7H_5O_3+C_2H_5NO_2=HC_9H_8NO_4+H_2O-$$

another part being discharged as salicylate by the kidneys. Salicin undergoes decomposition in the bowel and in the blood into saligenin and glucose:

$$C_{18}H_{18}O_7 + H_2O = C_6H_{12}O_6 + C_7H_8O_2$$
.

Saligenin is itself broken up into salicylous (HC<sub>7</sub>H<sub>5</sub>O<sub>2</sub>), salicylic, and salicyluric acids.

These reactions supply an explanation for the *increased* acidity induced in the urine, and may also account for the irritation sometimes set up in the kidneys, which often leads to albuminuria, and sometimes to hamaturia.

The physiological action is exerted on the heart and lungs, lowering pulse-rate and blood-pressure, and likewise the respiration, the arrest of which is the immediate cause of death.

Delirium, tinnitus, deafness, giddiness, and headache are the results of its action on the central nervous system, but the peripheral nerves are not affected. According to Lauder Brunton, collapse may sometimes be induced by sudden depression of the circulation. The stage of de-

<sup>\*</sup> Cf. Year-Book of Treatment, 1896; and Therap. Monatsch., January and April, 1895.

pression is preceded by increased cardiac action, flushing, perspiration, and fulness in the head (Mitchell Bruce).

Therapeutic Action.—The antipyretic power of the drug may be connected with its germicidal power; both of them are hitherto unexplained. It is noteworthy that the normal temperature is not appreciably lowered. relief of articular pain, so remarkable in acute rheumatism, is also without an explanation. One of the most important virtues of salicylic acid is its cholagogue action, which differs from that of other agents in increasing the fluid instead of the solid constituents of bile (Lauder Brunton), a circumstance which suggests its employment in cases of biliary sedimentation. Another not unimportant action is the inhibition of the later stages of pancreatic digestion, indol and skatol not being formed in its presence.

The Action of Salicylates in Gout.—The affinity which undoubtedly exists between rheumatism and gout contains the suggestion that an agent so powerful in the former should not be inoperative in the latter. That it is really useful in gout has been and is held by many good observers, but between them there is much difference of opinion as to the degree of relief obtained, and as to the stages suitable for this medication.

Germain Sée,\* who was an early advocate of salicylates, considered them superior to colchicum, and not predisposing, like the latter, to chronic gout-in a word, as valuable as in acute rheumatism.

Barclay† was satisfied that they did not act so quickly as in acute rheumatism, nor so well in gout as colchicum. He thought, however, that salicylate of sodium might be of use where colchicum lost its effect, or in cases originally rheumatic.

<sup>\*</sup> Progrès Medical, 1877, p. 745, quoted by Duckworth.

<sup>† &#</sup>x27;St. George's Hospital Reports,' vol. ix., 1877-78.

Duckworth finds it inferior for the relief of the urgent symptoms, and thinks that most physicians agree with him in this; but in a few cases where colchicum failed completely, marked benefit was obtained.

Among the many supporters of the salicylic treatment of gout, including Latham, Ralfe, Lecorché, and Bouchard, none has expressed so strong a belief in the drug as Haig, who, holding that rheumatism and gout are due to the same cause, excess of uric acid, concludes that they must be both amenable to the same remedy so long as it disposes of the offending principle.

Noël Paton\* has reported a diminution in the uric acid excreted, in opposition to the results of Lecorché and of Haig, who found an increase in the uric acid.

According to Lecorché,† it tempers the severity of the acute attack and lessens the pain, but does not shorten the malady, as it does in rheumatism. In chronic gout its use much increases the uric output. Tophi have been noticed to disappear; but the action is more marked on cartilaginous and ligamentous infiltrations.

The rationale suggested by Lecorché‡ rests upon analyses made in cases of rheumatic fever, which show a considerable excess in the excretion of urea, uric acid, and phosphoric acid.

Lecorché believes that it gives a stimulus to the vitality of organic cells, and to the 'disassimilation' of the nitrogenous substances, thus acting in a manner opposed to that of the alkaline bicarbonates and sulphates.

His doses are 4 to 6 grammes a day. And in chronic

<sup>\*</sup> Journal of Anatomy and Physiology, January, 1886, pp. 26-32, quoted by Duckworth.

<sup>+</sup> Loc. cit., p. 583.

<sup>‡</sup> Lecorché et Talamon, 'Action du Salicylate de Soude sur l'urée, l'acide urique et l'acide phosphorique de l'urine dans le rhumatisme articulaire aigu' (Revue Mensuelle de Med., Fév., 1880).

gout with visceral trouble (except interstitial nephritis) he continues this treatment for months, with a few days' interval after each fortnight, thus departing from the practice of G. Sée,\* who used 3 drachms daily for three days, then 2 drachms for three days, and repeated alternately the same periods and doses for three weeks.

He noticed that the increased excretion of urea, phosphoric and uric acid began after one or two days, and lasted for three or four days.

Duckworth, whilst not regarding salicylate of sodium as likely to supersede colchicum, recognises its value, which he attributes to the cholagogue and vascular depressing property which it possesses, and to its chemical interference with the formation of uric acid. Its mode of action is sometimes prompt and decided; but usually it does not give relief so rapidly as colchicum, and not for a day or two in any degree appreciable to the patient.

Haig's views deserve special attention. His high opinion of sodium salicylate rests upon the fact that, whereas other acids render uric acid less soluble, salicylic acid removes it as a soluble salicylurate, salicyluric acid being more soluble than uric acid.

'Thus, salicylates probably clear urates out of the blood without allowing them to do harm in passing through, and they thus free the blood from uric acid, and allow the blood decimal to rise.'+ 'Acute gout supervening in the night is quickly relieved by salicylate of sodium if given in sufficient doses. 'In rheumatism the doses administered are large and frequent-20 grains every two hours—why not in gout? In those cases in which the pain is of a traumatic and surgical kind, as when due to excessive exercise, salicylates are found to be useless; rest and fomentation are the remedies.'

<sup>\*</sup> Cf. Duckworth, loc. cit., p. 358. + Loc. cit., p. 42.

According to Haig,\* salicylates produce a considerable secretion of uric acid during the first and second days, but the amount of this initial output is never again reached. Subsequent quantities show oscillations, but tend to approach the normal proportion to urea, and sink below it as soon as the drug is stopped. After the suspension of the drug, retention of uric acid again takes place into the tissues, whence salicylic acid had removed it at first with great ease, and subsequently in diminishing quantities.

Haig lays stress† on the fact that salicyluric acid formed by the action of the drug on uric acid is much more soluble in slightly acid than in alkaline or neutral fluids.

The Limitations of the Salicylic Treatment, and its Contraindications.—The weight of the arguments thus ably set forth no impartial judge will fail to admit. We are unable, however, to adopt without reservation the conclusion towards which they tend. Even were salicylate of sodium to justify on further trial Haig's estimate of its power to check acute gouty arthritis when administered in sufficiently large doses, its employment in that affection must remain much more limited than in acute rheumatism.

Rheumatic arthritis itself is far from being always amenable to its administration; we frequently meet with cases in which for unknown reasons the salicylate fails to relieve even when combined with alkalizing doses of potassium bicarbonate. Disappointment may be expected with yet greater frequency in gout, the clinical history of which is made up of idiosyncrasies. We do not therefore venture to anticipate here the same proportion of success as among the rheumatic.

<sup>\*</sup> Loc. cit., p. 56.

Were gout chiefly prevalent among young adults with sound tissues and pliable vaso-motor mechanisms, the treatment in question might be more widely applicable. The class we have to deal with is the opposite, and demands the greatest caution in the use of remedies. This is fully recognised by such warm advocates of salicylates as Latham, Bouchard, and Lecorché.

Whilst renal susceptibility is the weak point in gout, renal irritation is the chief danger to be feared from salicylates. Here, then, is a major contra-indication which excludes all those subjects in whom the kidney is not absolutely sound. Many others are under a strong suspicion of renal instability; to this group belong patients presenting a high pulse tension and occasional albuminuria. A minor contra-indication exists in connection with them, and we should not lightly submit them to the risk of large doses. There remains a limited number, the selected few, in whose soundness we may feel the necessarv confidence. Yet even here we cannot feel sure of the result. In acute gout all heroic treatment is a risk. Too sudden a relief by internal medication may lead to the same complication as sudden revulsion by outward treatment, and experience shows that both lithium and the salicylates are not free from this form of danger. In short, the treatment of acute gout by large doses of the latter must still be regarded as experimental, even in those cases in which it is admissible, and on no consideration should any but the 'natural' preparation be prescribed. Meanwhile, a modified treatment of the acute attack by relatively small doses of sodium salicylate has been widely adopted by practitioners, with results which are reported as satisfactory.

When applied to chronic gout or to goutiness, the medication in question is free from the chief objections

which we have urged. Large doses are not so much required as perseverance in the use of the smaller supplies. Time is not a consideration. Each case can be studied at leisure. An intolerance of the remedy is disclosed before harm has resulted. And, lastly, an intermittent administration may procure the benefits of the treatment without any of its disadvantages. In this form the salicylic treatment is of much value, and is favourably endorsed with the personal testimony of patients belonging to the profession.

### BENZOIC ACID AND ITS SALTS.

The chemical behaviour and the mode of action of benzoic acid closely resemble those of salicylic acid. It shares with the latter the property of enabling any excess of nitrogen to be voided in acid urine as a soluble organic salt instead of in the shape of insoluble urates. Whilst, therefore, its acidifying power renders it of use in the treatment of vesical troubles associated with alkaline urine, it claims to be a valuable evacuant for the elements of uric acid in gout, especially valuable in those atonic forms where the administration of alkalies is undesirable.

As in the instance of salicylic acid, glycocine, which is regarded as a factor immediately concerned in the formation of uric acid, enters into combination with benzoic acid:

$$C_7 H_6 O_2 + C_2 H_5 N O_2 {=} C_9 H_9 N O_3 {+} H_2 O. \\$$

The result is hippuric acid, the salts of which are soluble.

On the strength of this chemical fact, and of the theory based upon it, the benzoates have been much used with apparently satisfactory results. The ammonium benzoate gives the maximum acidifying effect; but in gout the potassium and the sodium benzoates will be found more

suitable. Their administration has been strongly advocated in this country by Sir A. Garrod.

Sodium benzoate had also been recommended by Ure, Simonet, and Chalvet, Bence Jones, René Brian,\* and Ruken† (Lecorché). With the administration of benzoate of lithium Lecorché found a diminution in the uric acid excretion from 0.70 to 0.30, and in another case from 0.65 to 0.28.

Duckworth has likewise prescribed the lithium salt of benzoic acid, sometimes beneficially in chronic gout, in doses of from 8 grains to  $\frac{1}{2}$  drachm, and in combination with tincture of nux vomica. He reminds us of a valuable suggestion made by Golding Bird to combine with the benzoates the administration of phosphate of sodium.

Under the benzoic treatment a general improvement and a relative immunity from attacks have often been reported.

Whether these results are to be attributed to the chemical influence which has been suggested, or to some other mode of action, must remain for the present undecided.

# IODINE, SULPHUR, ARSENIC, AND MERCURY.

These bodies belong to the group of alteratives; their special function in therapeutics is concerned with metabolism, and in that capacity they are likely to be of service in an affection such as gout, which may be regarded as a deviation from the healthy type of nutrition. In reality they are of great value, especially in constitutional gout or goutiness. We need not dwell in any detail upon their

<sup>\* &#</sup>x27;Traitement de la Goutte par les Benzoates Alkalins.' Gaz. des Hop., 1856.

<sup>+</sup> Schmidt's Jahresbericht, Bd. cvii., No. 7, S. 21; 1860.

special virtues, which are well known and extensively utilized in the treatment of other diseases. None of them are specifics for gout, but in varying degrees they are all beneficial.

Mercury.—A considerable share of the usefulness of mercury in gout is due to its stimulating effect on the liver. As a purgative, the relief which it gives to the symptoms of portal congestion has rendered it deservedly popular among this class of patients, who so frequently labour under the depressing effects of hepatic torpor. Its mode of action as an alterative is ill understood. It is remarkable that, although readily absorbed into the tissues, it does not so readily leave them; and it has been found in all of them, and with special abundance in the liver. The slowness with which it is excreted is perhaps connected with its tendency to combine with albumen. Unlike some other metals, such as lead, arsenic, and antimony, it does not set up any recognisable changes in the viscera, nor in the other tissues short of mercurialism. Although the mercurial cachexia, with its varied results, is more rapidly induced in the subjects of renal disease, and the general symptoms of renal disease may suffer aggravation from a mercurial course, the kidney itself is not directly affected in its structure, as it is in lead intoxication.

The special liability to renal complication in gout, and the frequency of renal disease, suggest the greatest caution in the administration of mercury; but of its usefulness in some chronic forms of the affection there is not any doubt. Its diuretic action has been much insisted upon of late years; yet, according to Mitchell Bruce, it does not render the total excretions more abundant, and there is no positive evidence of its producing an increased metabolism.

Arsenic, easily taken up into the tissues and easily excreted, exercises a perceptible effect upon their metabolism, increasing the nitrogenous waste probably through an indirect stimulation of the process of oxidation, and inducing a conversion of their albuminous constituents into fat. This undesirable result belongs rather to the toxic than to the therapeutical action of the drug. With small doses, and with a systematic alternation of the periods of administration with periods of rest from the use of the drug, its beneficial advantages may be secured without any risk. In this way it has been successfully prescribed in chronic gout. The special influence exerted by arsenic upon the skin and upon the nervous system, the metal being abundantly found after poisoning in the grey matter of the cord, is an argument for its administration which would appeal to the supporters of the nervous theory of gout.

Sulphur is one of our most useful agents in gout as well as in chronic rheumatism. The rationale of its action is not thoroughly understood. Administered as an alkaline sulphide or as sulphuretted hydrogen, it is a reducing agent, and overdoses powerfully depress the nerve-centres, producing respiratory and cardiac failure. Sulphur itself in the uncombined state may partake of this property. At any rate, it is an alterative of undoubted value. Its stimulating effect upon the skin, including its diaphoretic action, has variously been regarded as as indication and as a contra-indication. Some forms of eczema are decidedly the worse for its use; nevertheless, it has sometimes been prescribed for this complaint. Individuals probably differ widely in their toleration. Similarly, its action upon the respiratory membrane needs careful watching. In the stage of hypersecretion bronchial catarrh is greatly benefited by sulphur, but when the excessive flow has

been checked, its continued administration may become a source of irritation.

Much of the efficacy of sulphur in these various directions is doubtless due to its purgative action, and to the relief which it affords to portal congestion and to hepatic engorgement. This is probably the secret of the great success of the treatment of gout by sulphur waters.

Iodine and the iodides are of decided value in gout, though we are at a loss to explain the mechanism of the relief which they give. Of their widespread alterative action, we possess varied and conclusive evidence, especially in connection with the lymphatic organs and their functions, and with the cardio-vascular system.

Upon the blood itself, iodine in toxic doses exercises a remarkable action, increasing its fluidity and dissolving some of the red corpuscles. Advanced kidney disease, which checks its elimination, is for that reason a decided contra-indication. The same remark applies to other forms of cachexia and to anæmia.

The great therapeutical feature of iodine is the extraordinary rapidity with which it travels through and permeates the system, loosely combining with available albumens, and more firmly with certain metals, such as lead and mercury, and speedily passing out of the body with the urine, with various glandular secretions, and partly also by exhalation from the respiratory mucous membrane. This swift transit, which stimulates and accelerates metabolism, has probably much to do with the beneficial effects obtained from its administration in chronic and subacute gout and in goutiness.

Iodine differs from the other members of this group in not perceptibly influencing the liver or the kidney; it may therefore be credited with a direct action on some of the processes of metabolism.

# IRON, THE VEGETABLE TONICS, AND GUAIACUM.

Little need be said of each of the members of this group. Their use is familiar to everyone. In gout it presents no risks or reservations which could not be pointed out in a very few words. They are best adapted to the sub-acute and chronic stages.

Guaiacum deserves special mention in connection with its well-marked efficacy in the myalgic and some of the neuralgic forms, and with its decided usefulness as a laxative and gentle hepatic, cutaneous, renal, and cardiac stimulant in all cases of chronic gout, and particularly in the atonic cases. It has been warmly advocated by Sir A. Garrod, and largely prescribed. Guaiacic acid (C<sub>6</sub>H<sub>8</sub>O<sub>3</sub>), which presents some analogy with benzoic acid, has been combined with metals. The guaiacate of lithium, administered in 2 to 5 grain doses, conveys some of the virtues of the drug under a smaller bulk; but powdered guaiacum or the ammoniated tincture are more reliable agents.

It is noteworthy, as bearing upon the yet undetermined mode of its beneficial action, that in toxic doses guaiacum acts as a gastro-intestinal irritant, and produces vomiting and purging.

Cinchona and its alkaloids are of the greatest use, and are hardly subject to any contra-indication in the non-acute stages. Although Dr. Haig has shown that, in common with their, caffein, and other nitrogenous bases, and with the acids and the metals, quinine tends to drive uric acid into the tissues, as a corrective for some of the more depressing evacuants of uric acid it is commonly prescribed with success, especially for continued use. Sydenham was of opinion that 'of simple medicines Peruvian bark is the best.'

Nux vomica and strychnine are also most useful as

general, as nervine, and as stomachic tonics. In their administration regard must be had to individual nervous peculiarities, and to the degree of renal efficiency. Imperfect renal emunction leaves the system overcharged with toxins, some of which are convulsants, and to these we should not add doses of a medicinal convulsant. As illustrating this point, which has special bearing in connection with the stagnation of waste material in gout, the observations of my friend Dr. T. Brushfield, of Wimbledon, possess much value. A large experience has convinced him that lying-in women, a class in whom catabolism is proceeding at a great rate, are peculiarly susceptible to strychnine, the physiological effects being produced in them by quite small doses. With these suggestions the handling of this important remedy may be left to the personal judgment of the physician.

Iron (and the same remark applies to manganese) is one of the most difficult remedies to administer with unerring success. It is not to be thought of whilst a recent acute attack is, as it were, within sight. As in the acute rheumatic state, so in the gouty, an untimely administration of iron will almost inevitably determine a fresh paroxysm. Dr. Haig explains this by the check placed upon the elimination of uric acid.

On the other hand, in many of the subjects of chronic gout and of goutiness, a mild chalybeate course is of signal service. The best mode of administration is that of the natural ferruginous waters drunk at the places where they flow. Next best is their use at home in more moderate quantities. Lastly, the milder preparations of iron may be prescribed to best advantage in association with a gentle alkaline treatment, with sulphur, or simply in their organic combinations as carbonates, tartrates or citrates. The management of the liver during the ferruginous course will need much attention and judgment.

### SYDENHAM'S ELECTUARY.

Stomachics are the most valuable of our tonics in gout. If gout is a disease of malnutrition, and if the latter is aggravated by the complication of dyspepsia, stomachic measures must stand at the head of all remedial medication. This was thoroughly appreciated by Sydenham, who, indeed, hardly admitted that gout could be influenced for good by any other medicines. 'For my own part, I prefer an electuary of the complex character of Venice treacle, wherein the mutual fermentation of the simples heightens their virtue, producing a tertium quid, of which the virtue, as a whole, is greater than the virtue of the sum of its elements. For the sake of beginners, I will publish the form which I most use. It is as follows:

' B.	
Root of	angelica,
"	sweet-flag,
,,	masterwort,
,,	elecampane,
Leaves	of mugwort,
"	lesser centaury,
,,	white horehound,
33	germander,
"	ground-pine,
,,	scordium,
"	calamint,
,,,	feverfew,
"	meadow-saxifrage,
33	St. John's wort,
11	golden-rod,

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Leaves of wild-thyme,

" mint,
" sage,
" rue,
" Carduus Benedictus,
" pennyroyal,
" southernwood,
Flowers of chamomile,
" tansy,
" lily of the valley,
" English saffron,
Seeds of pennycress,
" garden scurvy-grass,
" caraways,
Juniper berries—āā q.s.
```

'Collect the herbs, flowers, and roots at the season most favourable for their respective virtues. Dry, and keep in paper-bags until they fall into a fine powder. Take 6 oz. of each. Mix, and make up with a sufficient quantity of the best clarified honey and Canary wine. Make into an electuary of the due consistence—secundum artem. Two drachms to be taken night and morning.

'Or (if this cannot be had) use:

'R
Conserve of garden scurvygrass, \( \) iss.;
Roman wormwood \( \) \( \alpha \)

Make into an electuary. Two drachms to be taken twice a day.

Wash down with five or six spoonfuls of:
Sliced horseradish, 3iii.;

Garden scurvy-grass, xii. handfuls;

 $\left. \begin{array}{l} \text{Watercress} \\ \text{Brooklime} \\ \text{Sage} \\ \text{Mint} \end{array} \right\} \bar{a}\bar{a} \text{ iv. handfuls };$ 

The peel of vi. oranges; Bruised nutmegs, ii.; Brunswick mum, O.xii.

Distil in a common still until six pints are given off.'

Who knows but that in this lavish supply of the bright ornaments of our meadows some healing virtues may yet lie undiscovered? The lily of the valley, foxglove, and meadowsaffron itself, have waited long for a recognition of their value. The majority of the constituents of Sydenham's electuary are probably inert, but their number and variety are symbolical of the salutary effects of the fresh vegetable principles, and of a varied vegetarianism in diet, in the treatment of the jaded functions of the gouty.

We have now discarded all doubtful simples in favour of a few vegetable tonics which are decidedly efficacious, and especially of gentian, quassia, calumba, chiretta, and cascarilla. We should cling to their use in chronic gout by the side of that of the more potent bitter alkaloids. In dealing with atonic gouty dyspepsia, we may also wisely adopt Sydenham's suggestion in respect of carminatives, and combine with the bitters and the alkaline bicarbonates cardamoms, ginger, capsicum, and others.

The famous Portland powder, of which the recipe was purchased and published by the second Duke of Portland, is stated by Garrod to have consisted of equal parts of birthwort, gentian, ground-pine, and the tops and leaves of the lesser centaury; a drachm was to be taken fasting every morning, and subsequently smaller doses, but the treatment was to be kept up for twelve months. Sir A. Garrod gives an interesting account of the equally undeserved praise and censure lavished on this probably harmless preparation, which was really a variation on the form of treatment recommended by Sydenham, and long before by the ancients.

## CHAPTER XLIV.

# THE INTERNAL TREATMENT OF ACUTE GOUT.

The safety of the patient, the safety of the joint, and the relief of the local pain—these are, in the order of their importance, the objects of our treatment. To be successful, it must have regard to the fact that the acute gouty arthritis is the outcome of something more than a local irritation. Merely local measures could not cure the all-important constitutional cause, though the joint usually sets up the more urgent claim. According to the modern view of the march of events, it is too late to stop the action on the joint. Nevertheless, if the attack should be regarded as in itself curative, it would afford an opening for that help which constitutional treatment may give.

Happily, life is rarely threatened,\* except by the occurrence of severe complications in a heavily handicapped constitution. Nevertheless, the patient's desire for a treatment both prompt and active may lead to the employment of remedies necessitating a careful watch on the constitutional effects.

Between the other two indications there is no opposi-

<sup>\*</sup> Sydenham had a poor opinion of treatment in gout: 'Nay, more; I can confidently affirm that the greater part of those who are supposed to have died of the gout have died of the medicine rather than the disease.'

tion; what is good for the pain is usually good for the joint.

In each of its details the treatment must be adapted to the individual case, with due regard to age, to the presence or absence of albumen or sugar in the urine, to constitutional tendencies, and to the degree of severity of the attack. The following remarks apply to a sthenic attack occurring in an adult of average strength, and with sound kidneys.

The paroxysm almost invariably seizes the patient in bed, and when localized in the foot, keeps him there. The obvious indication is to save, by recumbency, waste of energy, and a dependent position of the limb. Few patients will fail to understand the paramount importance of the horizontal posture, even if their unrest should drive them from their bed to the couch.

The physician's attention is first directed to the relief of the local pain by the means to be presently described, whilst internal remedies are being provided.

#### THE INITIAL PURGATION.

The patient, just prior to the attack, may have had constipation, looseness, or well-regulated bowels. Where constipation has existed, quick-acting remedies are called for. Two or three grains of calomel should be administered, and followed up after the lapse of an hour by a black draught. In the case of previous regularity we should not lose sight of the constipating effect of severe local pain; but we can afford to employ the slower method of relief by means of a pill, supplemented by a dose of saline the next morning. Even after preceding looseness, constipation may be expected to supervene with the onset of the fit of gout, and much judgment will be needed in adapting the treatment to the special

requirement. Fractional doses of calomel administered in pill will best fulfil the hepatic indication without provoking an undesirable alvine flux. Half, or a third, or a quarter of a grain, repeated perhaps after an interval of two hours, will meet the varying necessities of cases; and if no spontaneous action should ensue, a mild saline dose may be prescribed in due course.

Among the advantages claimed for this method, not the least important is that it obviates the necessity for large initial doses of colchicum. The full benefit of the drug may now be secured from doses which will not expose the patient to the risk of undue depression or intestinal irritation.

The Choice of a Purgative.—Although calomel either in very small or in larger but quickly expelled doses is hardly ever resented, caution is needed in its administration. Scudamore prescribed calomel in combination with antimonial powder and compound extract of colocynth every second night, or even every night, in addition to a favourite morning draught containing extract of colchicum, with magnesia and magnesium sulphate. Sir A. Garrod, in view of the occasional intolerance of the gouty for mercury, is of opinion that 'in advanced gout it should be altogether avoided.'

As a substitute for calomel, where the physician's experience or that of the patient discountenances its use, podophyllin may be combined with the colocynth and henbane pill of the Pharmacopæia.

Colchicum as a Purgative.—Those who have regarded the benefits of colchicum as mainly due to its purgative action have sometimes pushed its uncombined administration till the action was fully developed, and the characteristic green stools were obtained; more often some other laxative has been prescribed with it. Sir A. Garrod's teaching has largely discouraged this practice. He insists that the value of colchicum does not reside in its purgative properties—a point we shall presently touch upon again.

Nevertheless, the experience of some practitioners will cause them to adhere to the early use of colchicum as an ingredient in an aperient draught, following in this the practice of Scudamore. A relatively large dose can in this way be given, and whilst safely expelled, may yet do some service in other ways. Sir Dyce Duckworth suggests that half a drachm added to a black draught 'may replace colchicum during the day.'

### THE INTERNAL MEDICATION.

Our description of the systematic medicinal treatment need be but brief after the remarks which have been made in preceding chapters under the heading of the various remedies. Much will have been achieved if the liver has been sufficiently influenced by our laxative measures, particularly if they should have included a full dose of colchicum. The action of the latter may be safely kept up by adding to any mixture prescribed doses of 10 minims of the wine. Unless the attack be unusually severe, the main treatment may with great advantage be conducted on the milder lines of refrigerants, diaphoretics, and antacids. An effervescing combination of 2 drachms of the solution of acetate of ammonium with 15 grains of citrate of potassium and some flavouring agent may be taken every four hours. Or sodium bicarbonate and magnesium citrate may be prescribed in the usual doses.

Opium\* is contra-indicated unless it be administered in the form of Dover's powder; but it will be better to order

<sup>\* &#</sup>x27;Nevertheless it will not be amiss to take a little laudanum in the evening if the pain be above bearing. Otherwise it will be better omitted.'—Sydenham.

for the night a draught which may be repeated without inconvenience if the pain should be excessive. For this purpose potassium bromide, tincture of hyoscyamus, and spirits of chloroform in camphor-water, is a useful prescription. Antipyrin, which is recommended by Dr. Burney Yeo, or phenacetin, may also be given in repeated doses.

In contrast with this bland treatment, we may refer to some more active methods.

Colchicum in relatively large and repeated doses is now seldom required. This practice has its disadvantages, to which we need not again refer.

Sodium salicylate in the large and frequent doses which afford quick relief to acute rheumatic arthritis is strongly recommended by Dr. Haig. We have no experience of this method. We have already dwelt on the objections to which it is open. Albuminuria and a fortiori kidney disease are absolute contra-indications. At the best, the renal function is under suspicion, and we feel diffident of any medication making heavy and continuous demands upon its excretory activity.

In small doses sodium salicylate appears to be well borne, and the milder attacks are often successfully treated in this way. Before its adoption the urine should be tested for albumen, and any symptoms of salicylism must be watched for during its administration.

Large doses of the alkaline salts are not desirable during the acute attack. The time has passed for their solvent action, which Sir W. Roberts, moreover, has shown to be problematical. Whilst no benefit can accrue from their use, their depressing effect is a strong objection.

Tincture of iodine is highly spoken of by Dr. Mortimer Granville, who prescribes it in 10-minim doses, with chlorate of potassium and chloride of ammonium. We believe in its efficacy in chronic gout, and in various forms of goutiness, but have not employed it in acute gout.

Whatever medicinal agents may be preferred, a most essential part of treatment is the free administration of fluids. The onset of diaphoresis is acknowledged as a comfort, and cannot fail to allay the feeling of feverishness and unrest.

#### THE DIET IN ACUTE GOUT.

At the onset and during the worst stage solids are not required, neither are they often acceptable. In this acute gout resembles acute rheumatism; in neither of them is there much appetite so long as the pain is severe. Yet we do not so often find in gout that complete anorexia which lasts for at least two or three days in acute rheumatism. In gout the appetite is often not absolutely killed. This must be borne in mind, together with the fact that the pain is peculiarly severe and exhausting, and that the hitherto luxuriously-fed stomach may feel the craving for stimulation.

Nevertheless, in the acute stage of sthenic gout nothing but good can come from restricting the diet to fluids: milk, variously diluted with hot water or effervescing water, koumiss or whey, barley-water or gruel, and perhaps some weak tea. The next day chicken-broth with thin toast will be a welcome addition; and in favourable cases there is no reason why, after twenty-four hours of the rigid fluid diet, light puddings rendered tasty with spices, and sweetened with saccharine, should not be allowed. Light farinaceous food is, however, the only kind suitable to this stage.

The return to a solid diet should be gradual. A little boiled fish, and a sago or tapioca pudding with dry toast,

should suffice for the single solid meal, which should be taken in the middle of the day. An egg for breakfast and some milk-pudding for supper may also be allowed. These rigid rules can only be relaxed when the patient is equal to a little exercise in the room, or to a drive.

The question as to alcohol does not arise in the ordinary case of acute gout, but should be considered in asthenic cases.

#### CHAPTER XLV.

### THE LOCAL TREATMENT OF ACUTE GOUT.

#### THE GENERAL INDICATIONS.

SIMPLE measures of nursing are of distinct value in providing for the support and protection of the limb. The patient's severe pain and restlessness, and our inability to subdue them immediately, lend importance to these lesser indications.

Position and Support.—On general principles elevation of the limb is indicated, although the relief thus obtained is slight compared with that afforded in ordinary inflammation. When, as in most cases, the foot is the seat of pain, the lower limb must be so arranged as to allow perfect freedom to the circulation, both at the bend of the knee and in the groin. This is essential for the relief of local congestion, and for the avoidance of any pressure on the veins, phlebitis being among the dangers to be guarded against.

The unavoidable restlessness of the patient also demands a certain freedom of movement, and this should be provided for; but when all has been done, it will be found that the patient will seek for himself the attitude of greatest relief.

The limb should be made to lie as softly as possible, so long as it is sufficiently supported. Water and air cushions are somewhat disappointing in their want of

steadiness, but they obviate much pain from shaking or vibration. Any rough contact is also to be guarded against, and the weight of the bed-clothes taken off by a large cradle placed over the limb.

Simple applications, such as cotton wool or flannel, are always grateful and safe. Their virtue is their warmth and lightness, and the exclusion of all draughts of air. Many are intolerant of any weight, and prefer for this reason fomentations to poultices; these, however, are often of use, and were praised by Sydenham: 'A poultice made with white bread, saffron, and a small quantity of oil of roses, has done me more good than aught else. Nevertheless, at the onset of a fit it did nothing. Hence, if the pain be very violent, the patient will do better by lying in bed until it have somewhat remitted than by using anodynes.'

Warmth and Moisture.—Both are beneficial. In applying warmth we never do harm, but assist nature in promoting cutaneous action, and the patient's feelings bear witness to this. Our policy is not to subdue abruptly the inflammatory swelling, but rather to relieve the tension of the tissues, and for this end moisture is also indicated. The most effectual means is the cautious employment of steam, and if simpler methods do not give relief, this may be resorted to, not, however, without the physician's supervision.

Simple Method of Steaming the Limb.—A local steam bath may be improvised in a few minutes with the aid of the following simple requisites: an ordinary kettle, to which is attached a good length of gas-tubing; an ample piece of india-rubber sheeting (a mackintosh garment may be turned to account); a common packing-box of suitable size converted into a cradle by knocking the two opposite sides out of it; lastly, a couple of garters or india-rubber

bands of proper size. The limb is to be carefully wrapped in flannel from the knee to the ankle, and a loose layer of cotton-wool placed over the foot and completely covered with flannel. The cradle having been fixed over the mackintosh and pillow which support the foot, a second piece of waterproof sheeting is spread over the whole, well tucked in under the sides of the pillow, and fixed by the garter below the knee. Before doing this, the end of the india-rubber tube, well protected from immediate contact with the skin by a thick layer of cotton-wool, is to be securely fixed to the under surface of the cradle at a distance from the foot. The foot end of the apparatus, left open at the beginning of steaming, is gradually closed. This is best done at the patient's own judgment, by drawing the waterproof partly or entirely over the opening. The duration of the steam bath need not exceed ten minutes in most cases.

#### THE LOCAL MEASURES OF TREATMENT.

Local Depletion.—The application of leeches, a sovereign remedy for many painful inflammatory affections, has been found comparatively useless in acute gouty arthritis. In this country Cullen seems to have been its last advocate. Scudamore, although still a partisan of the use of the lancet, and Todd, who was opposed to it, both agreed in deprecating local leeching. Since Sir A. Garrod's unequivocal disapproval of the method, it has probably rarely been practised. The objections which have been raised against it are chiefly based upon the disappointing results obtained, and upon the risk of superadding an erysipelatous inflammation to the gouty. Moreover, in a few reported cases an aggravation of the local symptoms, permanent weakness (Todd), early ankylosis (Garrod), or a metastasis of the inflammation, have been noted.

Local Blistering.—Some of the objections urged against the use of leeches are also applicable to the practice of blistering, which, however, has had eminent supporters. Sir A. Garrod considers blisters unnecessary in the early attacks, and restricts their use to asthenic cases with a tendency to effusion. Sir Dyce Duckworth adheres to the same view. Bearing in mind the possibility of complications, and the widely different manner in which even healthy skin reacts to the same blistering agent in different individuals, the wisest course is to avoid any risk, and to select some other form of local treatment.

Topical Applications. — The list of local applications vaunted or approved in practice is a very long one. They may be classified under the headings of anodyne, stimulant, alkaline, and astringent applications. Members of two or three of these groups may sometimes be combined with advantage. Colchicum, so efficient internally, has also been applied to the surface, but without definite results.

Astringents.—Of the use of astringents in local treatment the same may be said in principle as of the use of cold. The lessening of the local vascular fulness by any violent measures is not in agreement with our view of the requirements, and is not devoid of danger. Nevertheless, when coupled with the application of warmth and of sedatives, such astringents as a weak solution of acetate of lead or a warm infusion of astringent leaves may give considerable relief. In usual practice warm Goulard and opium covered with oil-silk is found to be satisfactory.

Anodynes.—The preparations of opium stand at the head of the list. Lotions containing laudanum are commonly resorted to, or laudanum may be sprinkled on fomentations or on poultices when applied. Morphia can also be used as an ointment or in solution.

The preparations of belladonna are also highly recom-

mended and extensively used by some. The glycerine of belladonna is a convenient form; or a bland ointment, such as the Pharmacopæial atropine ointment, may be preferred. Sir Dyce Duckworth speaks well of the combination of atropine and morphine in solution of oleic acid, which should be painted over the painful joint; he also refers to the local use of flexile collodium and of French chalk, but deprecates any agent likely to choke the sweat-ducts.

Cocaine has been recommended according to various formulæ as an ointment or as a liniment. Camphorchloral, ichthyol, and menthol have also been used.

Stimulant Applications.—The handiest of all applications are the warm spirituous lotions patronized by many gouty patients. The spirit and water is applied on flannel or lint, and covered with oil-silk. Such apparently unpromising remedies as iodine painted on the joint, or nitrate of silver applied or gently rubbed over the inflamed surface, have been resorted to by patients who have experienced benefit from them. They should rather be left to individual selection on the part of the latter than recommended by the physician in the absence of any previous knowledge of the effects personal to the patient. To the same class belong such remedies as the oil of peppermint, or the lotion of menthol mentioned by Duckworth.

Alkaline Applications.—These are of undoubted value in many cases. Weak solutions of the carbonate or of the bicarbonate of sodium, in the proportion of an ounce of the salt to a pint of water, are popular remedies; they should be applied warm. The relief obtained from them is greatly enhanced by the addition of laudanum, and is accelerated by a preliminary course of vapour carefully regulated as regards temperature, and suitably adjusted so as to take effect on the inflamed surface without causing

irritation. Or the joint may be packed with a warm alkaline and opium lotion ( $\frac{1}{2}$  oz. of crystals of carbonate of sodium, 2 drachms of laudanum, 10 oz. of water. Mix with an equal quantity of hot water; then pour some of the hot lotion over the part, which is packed in cotton-wool covered with oil-silk, and raised.—Burney Yeo).

The purpose of this form of treatment is different from that with which it is applied to the concretions of chronic gout. The inflamed skin is not in a condition to absorb appreciable amounts of any substance, even the most diffusible. On the contrary, our endeavour is rather to promote excretion, and in this respect warm moisture and alkalies are superior to all other agents, especially if, contrary to the rule, the sweat-glands should remain inert, in spite of the previous application of cotton-wool. Marked relief is given to the painful tension of the fibrous stroma, the pressure on the cutaneous lymphatics is lessened, and the natural flow within them, from which relief is ultimately to be sought, tends to be restored. At the same time, lateral pressure is taken off the painful nerve-endings, and their own structural elements are probably relaxed. It need hardly be pointed out that the wall-tension of arteries and veins is lessened, and circulation within them considerably favoured.

Ice and Cold.—The application of cold should be mentioned chiefly to warn against it. In the agony of their pain patients are occasionally driven to try this method. Hippocrates and Galen mention cold affusion as a means of relief; and, according to Heberden,\* Sydenham was in the habit of plunging his painful limb into cold water. Rothe† has within recent years revived the practice of

\* Quoted by Rendu.

<sup>† &#</sup>x27;Behandlung der Gicht mit Kalten Douchen:' Memorabilien, Heft 2, 1877 (quoted by Rendu).

systematic cold affusions and applications, and states that he has thereby relieved the pain and shortened the duration of the attacks.

In spite of this advocacy the practice is one to be strictly avoided. The dangers incidental to it have been sufficiently dwelt upon. Cold is invariably repugnant to the local feelings of the patient, and we have it on Garrod's authority that, when the sudden revulsion of the cold douche succeeds in allaying the inflammation or in mitigating the pain, this relief is but temporary, and the acute attack is not materially shortened.

An exception must be made in favour of the modified method of treatment by ice, as suggested by Sir W. Wade. In the belief that the pain is mainly localized in the nerves, and due to their inflammation, he suggests the application of ice along the lines followed by them, which are also those of the acute tenderness. The objections mentioned above do not apply here, since the greater part of the congested limb is not submitted to refrigeration. Ice in this case is used as a strictly local anodyne or anæsthetic, whilst it may help in subduing any existing neuritis or congestion.

The simplest method is to select a wedge-shaped piece of ice, the sharp edge of which may be made smooth by dipping into hot water, and, holding it in a thick fold of blotting-paper or flannel, to rub it lightly along the course of the nerve, much in the same way as a tailor uses his chalk. The application often gives great relief to the pain, and is not accompanied with any of that shock which, above all things, is to be avoided in gout.

#### CHAPTER XLVI.

# THE TREATMENT OF CHRONIC ARTICULAR GOUT.

#### THE CHIEF INDICATIONS.

This chapter will include a consideration of those cases in which subacute attacks of genuine gouty arthritis are of frequent occurrence and easily provoked, though the joints may not present permanent changes, and those in which permanent deformity has resulted, whilst the gouty tendency remains in active progress. Gouty cachexia, which also belongs to the 'chronic' group, calls for a treatment differing so widely from that to be described, that it should be considered separately. The treatment of goutiness and of its various visceral manifestations will claim separate chapters.

The cases in question constitute the majority of those which seek treatment for the relief of gout; and the greater part of the therapeutics of gout has reference to them.

In tophaceous gout and in crippling gouty arthritis an additional indication arises, that of the *local treatment of the joint*, for which in the remaining cases there is only an occasional need. The *constitutional treatment* is an indication common to the whole group, but which in its details varies with each set of cases. Thus, in all cases of confirmed gout the main indications have reference to the constitutional rather than to the local trouble. If the

process of nutrition can be restored to a healthy state, all the phenomena of gout, including the uratic dyscrasia, will be under control. The means to this end, foreshadowed in the chapters on the pathological and clinical aspects of gout, are:

- I. An improved excreting activity of the bowel, skin, and kidney.
- 2. A more active metabolism, for which the glandular organs, and particularly the liver, should be appealed to by medicines, and the muscular system by exercise and oxygen.
- 3. An improved digestion and assimilation, to be secured by diet, by hygiene, and by tonic remedies.

These broad outlines include in detail the use of the following agents: purgatives and laxatives, diaphoretics, diuretics, glandular stimulants, hepatic stimulants, cholagogues, alteratives (especially those capable of accelerating tissue change), and lastly, in addition to hygiene and diet, the important group of gastric and nervine tonics.

At the same time, we should not lose sight of the articular indication in connection with internal treatment, the cherished aim of which has been, for the last forty years, to dissolve the deposits of the biurate by chemical remedies. This therapeutic intention, which has never been perfectly fulfilled, is represented in our list of medicines by the alkaline group, and by some other alleged solvents of uric acid.

### GENERAL MANAGEMENT OF CHRONIC GOUT.

Chronic gout is not, like the acute attack, self-curative. So long as the circumstances which led to it prevail, it tends to grow worse. Its continuance is a proof that the sufferers have neither known how to ward off its approach nor how to check its progress. They are eminently in need of advice.

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Yet in the earlier stages, if they could act fully up to our present knowledge of treatment, gouty patients would need little medicine for their cure. They might be their own physicians if they could carry out with perfect fidelity the great rational indications. For this attainment time and patience are necessary. As stated by Sydenham: 'Be our digestive\* remedies what they may (medicines, diet, exercise), they must not be taken by-the-by, but must be steadily and diligently adhered to. In gout, as in other chronic diseases, the cause is a change and new nature of the system. Now, no sensible man can believe that light and momentary change can remedy this. The system must be transformed. The man must be made anew.'

The physiological preventives and the physiological cures for gout are: a sufficiently warm climate, a vegetarian diet, and a perfect hygiene. Each of these alone would avail much, but success can only be assured by their combination.

The great majority of our patients are unable to carry out any of these methods of self-cure. It is for us to devise for them a modified treatment, in which medication seeks to make up for that which is unattainable by simpler means.

Our management should include as much of these main indications as each case can afford. The climatic advantage may be partly secured by residence, at least for part of

<sup>\*</sup> Sydenham explains thus what he means to be understood by a 'digestive': 'Whatever helps Nature in the discharge of her functions, either by comforting the stomach, . . . or by strengthening the blood to the due assimilation of the chyle brought to it, or by restoring the solid parts in such a manner as to fit them for the conversion of the juices destined for their growth and increase into their own proper substance, . . . whether medicine, diet, exercise, or change in the non-naturals, is a digestive.'

the year, at some of our warmer health resorts. Of these there is a choice. The Isle of Wight, Ilfracombe, Torquay, Southsea, St. Leonards, Worthing, and Brighton, are among the best known.

For those who can travel, the winter spent in Egypt or the Riviera, in Morocco or Algeria, in Spain or Italy, or the summer spent in Switzerland, will fulfil the requirement. Irrespective of the influence of climate, much good accrues from the renovating effect of varied scenery and surroundings, of novel impressions, and of the unforeseen which is more frequently happening than in the monotony of home-life. All these act as stimulants to the nervous system, and react favourably on the functions.

In itself the interruption of the routine of home, even at the cost of some pet comforts, is most beneficial. A winter tour to Northern India, to New Zealand, to the Southern States, especially Southern California, or Mexico, or to the West Indies, is much to be recommended. In America and in New Zealand a valuable course of thermal waters can be combined with the tour.

Whilst discussing the question of travel, we may briefly refer to that of balneology. A yearly visit to some mineral spring forms part of the programme of treatment, and whenever manageable should be carried out. We shall enter into further details in the chapter on medicinal springs.

The dietetic indication of vegetarianism is in the vast majority of instances a dead letter. Fortunately, very good results can also be obtained on a mixed diet; but on this plan the patient is much less protected, and more open to the temptations and risks from which a sterner rule would have freed him. Selection as to quality and quantity becomes a complicated matter, and the moral check of a dietetic prescription has to be resorted to.

The subject of diet will be fully dealt with further on, and with it that of *alcohol*, an important detail in our general management of chronic gout.

The hygienic indication in its most complete form, which will be described in a special chapter, can seldom be carried out. Muscular exercise is its chief essential, but mental exercise should not be excluded. In opposition to a prevailing view, Cantani recommended vigorous mental activity. It should never be carried to the point of exhaustion, nor take the place of the needful muscular exercise.

The physician's advice will be needed to apportion in each case the suitable amount of exertion, and to regulate all matters of hygiene, and particularly those relating to an open-air life.

Unfortunately, the advanced stage of the affection or unavoidable circumstances too often stand in the way, and chief reliance must be placed on medication and careful dieting.

## MEDICINAL TREATMENT.—THE LAXATIVE AND SALINE TREATMENT.

So long as a mild laxative treatment can be kept up without debilitating the subject, we may hope to keep the morbid tendency in check. Our choice of remedies is large. We may divide them into three groups: the simple aperients, the hepatic and glandular stimulant aperients, and the muscular stimulant aperients.

The simple aperients are represented by ordinary salines devoid of any special hepatic function, such as the citrates of potash, soda, and magnesia, and the effervescing citrates and tartrates so largely used by the public under various names.

The muscular stimulant laxatives have two important

representatives in cascara and in guaiacum. The latter is particularly useful, and has been largely prescribed by Garrod. It has the advantage, in addition to its purgative action, of definitely relieving muscular and other pains in gout. The use of cascara is now well known.

The list of hepatic stimulant laxatives is a long one. Their vegetable representatives are colchicum, colocynth, podophyllum, rhubarb, aloes, and euonymin, which may be with advantage combined with hyoscyamus. The mineral group contains sulphur, a most useful and safe remedy for a continuance, most convenient in the form of Garrod's compound sulphur tablets, and rendered comparatively palatable in the compound liquorice powder; the mercurial preparations as occasional correctives; and the stimulating salines, and particularly the combination provided by nature in the Sprudel spring at Carlsbad, which may be recommended for more or less habitual or for recurrent use.

We shall refer under a different heading to the laxative and purgative plan temporarily adopted at mineral stations.

The simple saline treatment advocated by Garrod often suffices to regulate the hepatic and intestinal function, and it will be well if purgatives can be put aside for occasional use only.

Magnesia and its carbonate were praised by Scudamore, and are of undoubted use as mild antacids. To the virtues of the sodium bicarbonate we shall revert presently. Lithia and its salts, and, above all, bicarbonate of potash, have been largely prescribed, and the judicious and temporary use of the latter has not met with any serious objection, though we cannot speak favourably of its continued administration in all cases.

#### THE DIURETIC AND DIAPHORETIC TREATMENT.

Diaphoresis as obtained by muscular exercise will be appropriately considered under the heading of hygiene. The diaphoretic agents suited to chronic gout are in great part identical with, and partly also complementary to, the diuretic measures. The warm bath which predisposes to sweating, and the hot-air and vapour bath which induce it, are direct instalments of renal treatment, through the relief which they afford to the function of the kidney. The hot-air bath may be, when it is not contra-indicated, of signal service in albuminuria and kidney disease dependent upon gout.

The treatment of the kidney in chronic gout has a double aspect. The careful avoidance of irritating beverages and food, and the free use of diluents, are, together with freedom of the cutaneous and intestinal functions, the chief sources of relief from overpressure in the renal department. Diuresis is promoted by the salts of potassium and of lithium, now largely used; their administration in the dilutions recommended by Garrod adds much to the effect.

A safe and effectual diuretic is pure water taken in sufficient quantity. Special advantages belong to the use of hot water (a tumblerful on waking, at bedtime, and an hour before the mid-day meal), which stimulates the skin and the alimentary mucous membrane, as well as the kidney.

#### THE ALKALINE TREATMENT.

The method which endeavours to ensure the solubility of the excess of uric acid present in the blood in chronic gout, and to dissolve the biurate deposited in the joints and tophi, took its origin in chemical observations from which inferences were drawn far in excess, as Sir W. Roberts has shown by further chemical research, of the actual facts. Are we to conclude at Sir W. Roberts' suggestion that the treatment in question is altogether useless, and that the persistence of tophi and the recurrence of gouty seizures in spite of alkalies administered continuously in doses sufficient to keep the urine alkaline are arguments against the further use of alkaline remedies? A single adverse observation of this kind suffices to raise the strongest doubt as to the solvent virtue once attributed to them.

Nevertheless, if we were to forget the existence of uric acid, we might yet find in their general properties, which have been already described (cf. p. 369), ample justification for their employment. Besides uric acid, we observe in gout a general acidity which needs to be controlled, a retention of waste products which need elimination, a slowness of metabolism which requires stimulation. Alkalies, and specially potassium bicarbonate, are of value as local and general antacids, as diuretics, and as alteratives, and their moderate doses are decidedly beneficial.

In giving up the hope of dissolving the biurate, we need not sacrifice these advantages, but we are freed from the chief excuse for a continuous alkaline treatment, to which there are valid objections. We are indebted to Sir W. Roberts for repeating with renewed force Sir A. Garrod's original recommendation not to alkalize the subjects of chronic gout to the extent of keeping the urine alkaline. The depression which this induces is detrimental, and the same remark applies in many cases to the habitual use of potash and lithia water. These waters are too often regarded as mere articles of diet. They should be prescribed by the physician, not by the patient.

Sodium bicarbonate, for reasons which we need not re-

peat (cf. p. 379), is not usually resorted to for the purpose of rendering the urine alkaline. Its wide range of usefulness in practical therapeutics as an antacid and as an hepatic stimulant would seem to point to its special value in gout, and we could ill afford to spare it unless it were definitely shown to be harmful. That it promotes the precipitation of the biurate is the inference derived from Sir W. Roberts' experiments, and a suspicion to the same effect was long ago expressed by Sir A. Garrod. We think that this objection is partly theoretical, and should not deprive us of the legitimate use of the remedy. In chronic gout it has been and is largely used, not only on the Continent, but in this country. Some patients who have experienced its benefits take it regularly in the morning or at bedtime freely diluted, and gouty dyspeptics are largely dependent upon it for relief. At Vichy and Wiesbaden acute attacks are known to occur during the use of the mineral waters, but this result is not limited to the sodic waters, and probably has some other explanation.

In practice we can afford to lose sight of the solvent power of potassium bicarbonate for uric acid, and of the production by sodium bicarbonate of an insoluble biurate, so long as we can deal successfully with the more essential requirement of limiting the supply of uric acid itself.

In conclusion, we adhere to the view that the bicarbonate and citrate of potassium are of use as antacids, as diuretics, and as alteratives; that their doses should not be large, nor their administration long continued, but, if necessary, frequently renewed. Cases of marked acidity and showing a tendency to sthenic articular attacks are those calling for this treatment.

Sodium bicarbonate as an antacid is suited to asthenic cases, and to the sufferers from dyspepsia with torpid

liver. Here, again, the intermittent administration is preferable, and it is advisable to limit the strength of the doses and their frequency.

#### ALTERATIVE REMEDIES ACTING ON URIC ACID.

This important group comprises the salicylates and the benzoates. They share the valuable peculiarity of allowing the urine to remain acid, whilst increasing the elimination of uric acid. The formation by them of salicyluric acid and of hippuric acid respectively with the elements of uric acid has been described in preceding pages. Their beneficial action is not limited to this function. Benzoic acid is a valuable stimulant for the mucous membranes, and salicylic acid in combination with sodium acts as a most efficient cholagogue, in addition to its antiseptic property. Their indications in individual cases of chronic gout are thus clearly marked out. For subjects in whom any depressing treatment is to be avoided, and whose kidneys are not above suspicion, the benzoate of potassium may be administered in doses of a scruple, combined with a drachm of succus taraxaci and fifteen drops of spirits of chloroform. In other cases this treatment may be made to alternate for periods of a week or a fortnight with the saline treatment. Guaiacum may with advantage be combined with the benzoate.

Sodium salicylate is probably one of our most useful drugs in chronic gout, but its use must be restricted to cases free from renal disease. Lecorché and Haig, its strenuous advocates, have both found, soon after its first administration, a marked temporary increase in the amount of uric acid in the urine; this is followed after three or four days by a progressive decrease. The best results are obtained, according to them, by a continuous administration, for prolonged periods, in daily supplies of

60 grains or more. Lecorché finds that it not only decreases the amount of uric acid in the blood and lessens the liability to attacks, but that it promotes the absorption of the deposits. Haig is also a strong believer in its efficacy in lessening the accumulation of uric acid in the system. Its use should be combined with careful attention to diet and hygiene.

#### GENERAL ALTERATIVE REMEDIES.

The beneficial action of the members of this group is not exerted directly on the uric acid, but on the general metabolism, and in the case of some of them on the liver.

Colchicum was formerly prescribed in chronic gout by Sir Henry Holland, and by some other physicians, in a continuous fashion, as a preventive. Long before the introduction of the salicylates, Sir A. Garrod had expressed his disapproval of that practice, thinking that it would be better to reserve it for the immediate threatenings of an acute attack. We are now much less dependent upon its use than ever before, even in acute gout, and its continued employment as a prophylactic in the chronic affection is probably never suggested.

Iodide of potassium and iodine are, next to the drugs which have been mentioned, our most efficacious remedies in chronic gout, and the iodide has long enjoyed a well-deserved reputation. It is specially useful in cases presenting subacute and lingering swellings of the joints with some effusion, in the painful gout of the sole and of the heel, in the myalgic complications of gout, and in the neuralgiæ. In all these conditions, in order to obtain the full benefit of the treatment, the dose must be raised above that recommended by Sir A. Garrod (3 grains) in his remarks on the continuous administration. With

this, as with all other drugs in chronic gout, we must watch the results and gain the assurance that the excretory power of the kidney is equal to the task put upon it. Advanced kidney disease is a contra-indication, the imperfectly excreted drug causing irritation of the skin and an iodine rash. Dr. Burney Yeo mentions, however, good results in cases of 'albuminuria, with well-marked vascular and renal changes,' from the daily administration of from 15 to 30 grains. Where the albuminuria is functional, or the kidney changes not of the incurable interstitial variety, it may be desirable to obtain for the kidney itself a share of the wide-spread beneficial activity of the drug.

In cases free from renal complication, the treatment may be continued for long periods, the doses not exceeding 15 to 20 grains daily. Periodical interruptions do not interfere with the usefulness of the treatment.

The main indications for the administration of iodide of potassium are fulfilled in a higher degree by the tincture of iodine. Dr. Mortimer Granville has insisted on the value of this preparation even in acute gout. In chronic gout, especially that which affects the fibrous structures in and around the joints, the writer can strongly recommend its use in combination with iodide of potassium. He has found great benefit from it also in the painful affections of muscles and nerves. In the tophaceous variety it should also be tried, the indication being here to improve and modify the general metabolism rather than to influence the biurate deposited. The stimulating and 'warming' action of the free iodine on the nerves and mucous membranes is of great value. The dose will vary with individual cases, and according as the iodide is or is not prescribed at the same time. Five to ten minims three or four times daily would be a safe amount to prescribe in ordinary

cases, but this is often exceeded by the writer where a stronger effect is required. The tincture becomes almost palatable with the addition of some elixir of orange.

Guaiacum\* ranks high among the active remedies in chronic gout. The relief which it gives to the painful affections of the fibrous tissue and to the myalgiæ is a proof of its usefulness. Where iodide of potassium gives relief, guaiacum is also efficacious; they may with advantage be combined: the writer commonly uses them in this way. In the fluid form the insolubility and the colour of the drug are an objection, but it may conveniently be taken as a powder in cachets, or in the shape of tabloids.

Sulphur is another agent of great and acknowledged value in chronic gout. It is unnecessary to dwell upon its use here, since we shall again consider it in connection with mineral waters. Many sufferers are unable to visit the baths and drink the water. For them the administration of sulphur in mixture, cachet, or tabloids (Sir A.

- \* Sir A. Garrod, in a paper read before the Royal Medical and Chirurgical Society on May 26, 1896, has again expressed the very high opinion of the value of guaiacum which he has derived from a long experience. 'He thinks that he has been successful in establishing the following points in regard to its action:
- '1. Guaiacum is innocuous, and may be taken for an indefinite period of time, and looked upon as a condiment rather than as a drug—as harmless as ginger or any other condiment.
- '2. Guaiacum possesses a considerable power, but less than colchicum, in directly relieving patients suffering from gouty inflammation of any part; it may be given whenever there is but little fever.
- '3. Guaiacum taken in the intervals of gouty attacks has a considerable power of averting their recurrence; in fact, it is a very powerful prophylactic.
- '4. Guaiacum does not appear to lose its prophylactic power by longcontinued use.
- '5. There are a few persons who cannot readily continue the use of guaiacum; for such cases there are other drugs whose action is in some respects similar as prophylactics—perhaps serpentary is one of the most powerful of these.'

Garrod's 5-grain compound sulphur tabloids are specially useful where the aperient effect is desired), will be a ready substitute, though nothing will replace the general benefit conferred by the change of surroundings and of conditions.

Mercury is too important an alterative not to deserve a trial where other remedies fail. For reasons upon which we need not dwell again, it cannot be widely recommended. Scudamore laid stress on the evils apt to follow its injudicious employment, and Garrod states that, as it possesses no controlling power over gouty inflammation, it should not be prescribed otherwise than as an immediate cholagogue.

The administration of fractional doses, such as  $\frac{1}{8}$  grain of calomel or 15 minims of the solution of the perchloride, is free from the danger of causing any mercurialism, and it has been well borne and productive of benefit when continued for a few days. In some cases where anæmia is marked, and iron is not otherwise well assimilated, the addition of a small proportion of mercury may lead to the best results; but it is never desirable to submit any patient to a prolonged course of this treatment, and the indication only arises when the hepatic functions cannot be improved by other means.

Arsenic is of less value in chronic gout than in rheumatoid arthritis, and is better suited to the treatment of the nervous disorders incidental to goutiness than to the articular form. Nevertheless, arguments in favour of its use have been derived from its undoubted action on metabolism and on the nutrition of epithelial and nervous structures, and from the existence of a nervous element in all forms of gout. Again, the presence of minute doses of the metal in various mineral waters which have been found beneficial has suggested its independent employment. In cases where special indications can be traced,

whether in the cutaneous, the nervous, or the alimentary system, and where the kidneys are in a healthy state, the remedy might be safely given a trial with the usual precautions.

## THE TONIC TREATMENT DIRECTED TO THE BLOOD AND TO THE VISCERAL FUNCTIONS.

We have dwelt incidentally upon the functions of the liver and of the kidney.

The treatment of the cardiac symptoms arising in chronic gout will be discussed under a special heading in connection with goutiness. We may merely refer to the distinction elsewhere drawn between the organic group of affections which are more likely to be met with in those advanced in years, though not limited to old age, and those of a partly, if not wholly, functional character, which are capable of considerable relief, or even of complete amendment.

The Treatment of the Stomach.—Without the basis of an efficient digestion all medication is futile. In that sense the stomach claims our constant attention in chronic gout. The improvement of the digestion is the essential means to an improved assimilation and metabolism. It is best secured by hygiene and diet. Deferring these subjects and that of the aggravated dyspepsia of goutiness for separate consideration, we must allude to the treatment of the minor gastric disturbances which we are, in chronic gout, constantly called upon to correct. They resolve themselves into acidity on the one hand, and want of tone on the other. The acidity is to be subdued by the mild alkaline treatment. Bicarbonate of potassium will sometimes be necessary; but it is the privilege of sodium bicarbonate to suit both the acid and the atonic varieties.

The extreme acidity due to unhealthy fermentation of food calls for the administration of nitro-muriatic acid.

Even in the absence of any pronounced dyspepsia, we should treat the debility of the stomach, and our tonics should be those which best suit the digestion. The simple bitters are generally appropriate—cascarilla, quassia, chiretta, colombo, gentian; and the stronger bitter tonics—quinine, nux vomica, or strychnine—may be used in alternating succession. The addition of some carminative or aromatic, such as ginger, capsicum, cardamoms, cloves, is usually an advantage.

Serpentary combines the aromatic with the bitter tonic property, in addition to diaphoretic and diuretic properties, which have led to its employment in chronic rheumatism. Sir A. Garrod\* has recently stated his belief in the power for good of this drug in articular gout itself, particularly in the gouty inflammations of elderly subjects, and has hinted at its possessing some prophylactic action analogous to that of guaiacum.

This gently stimulating and tonic stomachic treatment remains practically the same as that adopted by Sydenham, whose long prescription is suggestive of the value which he attached to gastric tonics, and imitated in the preparation of various specifics, such as the Portland powder, and, more recently, the Pistoja powders.†

The remaining indication is to treat the anamia where it exists. Most often exercise, sunlight, and pure air are amply sufficient, and anamia suggests their more liberal use. In subjects deprived of these advantages iron may be needed; but its administration is not always a simple matter: the liver has to be reckoned with. For this reason

<sup>\* &#</sup>x27;Proceedings of the R. Med. and Chir. Soc.,' May 26, 1896.

<sup>†</sup> Compounded by the R. R. Benedictine Sisters at Pistoja, Tuscany (Burney Yeo).

the milder chalybeate mineral waters are found the most successful, especially if drunk at the health resorts; but they are also available as table waters.

If prescribed as medicine, the milder preparations should be selected. It may be desirable in some cases to alternate the administration with short courses of arsenic, or the effect of both metals may be combined, as in the arseniate of iron pill  $(\frac{1}{12}$  grain or  $\frac{1}{8}$  grain), which has often been recommended, and is thought to be a beneficial as well as a safe remedy.

#### CHAPTER XLVII.

# THE LOCAL TREATMENT OF CHRONIC GOUTY ARTHRITIS.

The Value of Local Measures in Chronic Gouty Arthritis.—
The importance of obviating the crippling effects of gout is appreciated by patients, and must be steadily borne in mind by the physician, who must be the judge of the extent to which movement is to be combined with rest to the joints affected. The skin of the gouty limbs needs careful attention; this indication includes the treatment of the local adema. Lastly, the management of the tophi and of the intra-articular deposits requires special care, and their surgical treatment is one of the questions for discussion.

Relatively trivial measures may effect much by assiduous use, but they are most efficacious when resorted to early. This is a sufficient excuse for dwelling upon details, which are not in the event as trifling as they might at first appear.

### POSITION, PASSIVE MOVEMENT, AND MASSAGE.

The position of the limb is not a matter of indifference where the articular swelling is considerable. By relieving local venous congestion, and promoting a free lymphatic drainage, habitual elevation of the part may lessen the rate of uratic deposition; it certainly counteracts the stagnation inseparable from disuse.

The local ædema, which is apt, in atonic subjects, to linger about the gouty joints, is best treated in this way; but the circulation may be aided by the lateral support of an ordinary gauze- or light flannel-bandage. Where it is persistent, the hot douche, followed by sponging with a cold, strong solution of common salt, was recommended by Hume, and found of much value by Garrod. Judicious rubbing or massage frequently applied may answer every purpose. Both forms of treatment are combined at the spas frequented by the gouty.

The full advantage of posture can only be obtained by raising the limb considerably, and by securing complete freedom of the large veins at the flexures.

Rest and Movement.—Both are useful, but they should be duly apportioned. We are sufficiently imbued with the necessity of rest for inflamed structures. In gout we have perhaps overlooked the opposite indication, which has long been recognised in the treatment of rheumatoid arthritis. The latter shows, even in the semi-acute stage, marked tolerance for passive movement, in spite of the pain which is inseparable from it. Movement of the gouty joints, in spite of its desirability, has been regarded as practically contra-indicated in the majority of cases. Sir W. Wade's observations have thrown new light upon this question. They show that even during the acute stage the bones entering into the formation of the joint can be freely manipulated and moved without causing any pain, provided no pressure is made on the tender spots external to the joint.

This has an important bearing upon the treatment of the chronic condition. *Passive movement* applied with gentleness and care at an early date after the subsidence of the acute symptoms would obviate the subsequent stiffness and the occasional occurrence of ankylosis. Massage should next be called to aid, and this may be usefully combined with the preliminary administration of a local warm bath, or, better still, of a local vapour bath which allows the limb to be raised for the relief of the local congestion.

At a later stage, when the patient is able to go about, massage should be administered in its most efficient form, according to the Aix plan, under a stream of thermal water. This method has now come into universal use, and can be applied at several of our own balneological stations. The internal use of the sulphurous waters is supposed to materially assist the local treatment.

#### THE LOCAL MEDICINAL TREATMENT.

Remedies have been locally applied for the treatment of the skin, for the relief of the articular stiffness, and for the solution of the tophaceous concretions.

The skin suffers not only through the general gouty malnutrition, but through want of proper exercise, and from the stretching which it undergoes. Passive exercise is to be supplied by friction, combined with the use of gently stimulating embrocations. Often, however, the integument is so delicate or tender that simple or camphorated oil is the only suitable application.

The articular stiffness and thickening call for rather stronger liniments, when they can be borne by the skin. Small blisters have been occasionally found of advantage by Garrod. Usually they are best avoided. Simple camphor liniment, or the compound camphor liniment, or liniments containing turpentine, carefully used, or iodine painted over the joint, will produce sufficient counter-irritation. A safe and useful application is the soap and iodide of potassium liniment gently rubbed in and worn over the part at night.

The solution of the concretions by the local application of alkalies was definitely advocated by Scudamore on the strength of the solvent power of potash for uric acid. He recommended as an application equal parts of liquor potassæ and of almond milk. The same principle was adopted by Garrod, to whom we owe the safer and more effectual treatment by lithium carbonate solution, in the proportion of 5 grains of the salt to I ounce of rosewater. This is suitable for continuous application under oil - silk, and has been found remarkably successful, causing in some cases the entire disappearance of the deposit. A popular remedy based on the same principle is the application of a warm solution of sodium carbonate; but even solutions of potassium carbonate, originally tried by Garrod, were found less efficacious than the lithia treatment.

The introduction of lithium by electrolysis has recently been suggested by Labutat.\* A similar method had previously been proposed by Edison.†

Solutions of piperazin, lysidin, and other similar bodies, may perhaps be found serviceable as topical applications.

#### THE SURGICAL TREATMENT.

Any surgical interference with joints affected with concretions or with late arthritic changes has always been regarded with disfavour. It must be admitted that many surgical questions which had been considered closed need to be reopened and to be looked at again from the altered standpoint of antiseptic surgery. Gout will probably not form an exception to this; but it is doubtful whether the decisions arrived at on further consideration will much

<sup>\*</sup> Gaz. des Hôpitaux, 1894, vol. lxvii., p. 1318 (quoted by Dr. Archibald Garrod, Year-Book of Treatment for 1896).

<sup>†</sup> Cf. Year-Book of Treatment, 1891, p. 158.

differ from those already given. An impression has prevailed that any wounds inflicted in the neighbourhood of gouty joints show an imperfect tendency to heal. On the other hand, Dr. Ord ('St. Thomas's Hospital Reports,' 1872) refers to the opposite tendency as having been observed by him, and gives a remarkable instance in point of a joint completely healing after the spontaneous discharge of a very large amount of unhealthy débris and There can be no question that the uratic deposit. vitality of tissues is depressed by gout, and that they are liable, not only to the special inflammation which we recognise, without quite understanding it, as 'gouty,' but also to erysipelas; the supervention of the latter is regarded as the main danger to be dreaded as the result of surgical interference.

In the ear, tophi may be punctured and slowly evacuated without any serious risk. In the vicinity of joints, this proceeding, as pointed out by Garrod, is hazardous, and may lead to prolonged suppuration, not only in the tophi operated upon, but in the joint with which they sometimes communicate. Although small incisions have often proved harmless, and have been the means of diminishing the size of the accumulations, the operative treatment is not one to be recommended, even with the help of antiseptic precautions.

When *spontaneous ulceration* takes place over a large concretion, the continuous application, under an antiseptic dressing, of the lithium carbonate in a boracic acid solution will fulfil a double purpose, and may be the means of rapidly diminishing the size of the swelling.

#### CHAPTER XLVIII.

# TREATMENT OF METASTATIC GOUT OF THE VISCERA.

WE shall limit the present remarks to the acute visceral crises distinctly traceable to the influence of an abrupt cessation of the acute arthritic symptoms, in contradistinction to the visceral complications observed in the state of goutiness, which are usually independent of any declared gouty attack in the joints. The treatment of the latter is considered in separate chapters.

Retrocedent gout is, fortunately, not common, less common now than formerly; and we need only refer to its three chief varieties: the gastro-intestinal, the cardiopulmonary, and the cerebral.

#### THE GASTRO-INTESTINAL FORM.

An obvious indication has reference to the cause of the trouble. It is applicable to all the varieties of retrocedent gout; and the same treatment is called for in each of them. We should endeavour to induce a renewal of the gouty inflammation in the joint from which it has disappeared. The simplest method is to apply mechanical irritation to the articular surfaces by passive movement of the joint, combined with some pressure—a proceeding the harshness of which is justified only by the critical state of

the patient. Superficial counter-irritation is also to be applied in the shape of the mustard foot-bath and mustard-leaves. Blistering is not called for, as it adds a trouble-some local complication to existing difficulties.

Meanwhile, the first of the symptomatic indications is the intense depression of the patient. Stimulating remedies are required. Brandy will probably have been administered, and its cautious use may be sometimes continued; but there are obvious objections to its unlimited employment, and commonly the stomach will refuse to retain it. Sal volatile and ether, reinforced by carbonate of ammonia, may be administered in chloroform-water; or they may be prescribed in an effervescing draught, which should not be too bulky.

If the stomach should be intolerant of these remedies also, we are able to fall back upon the use of smelling-salts, the subcutaneous injection of ether, and the rectal injection of brandy, of coffee, or of a solution of caffein. In this way the necessary stimulation can be secured in spite of the vomiting.

Another urgent indication is the often severe gastric pain. This is to be met by the local application of wet or of dry fomentations, sprinkled with two teaspoonfuls of laudanum. If very severe, the pain may call for the subcutaneous injection of a quarter of a grain of morphia. Sir A. Garrod recommends counter-irritation to the epigastrium and left hypochondrium.

Vomiting is to be promoted, according to the same authority, by diluents. There does not seem to be any object in keeping it up after the irritating gastric contents have been discharged. The best way to subdue it is to allow the stomach absolute physiological rest, and to keep up the strength by stimulants administered per rectum.

If there should be much flatulency, ether capsules, fol-

lowed by a draught of water as hot as can be borne, will probably cause the partial expulsion of the gas, whilst acting as a temporary stimulant.

If there should be any constipation, this should be relieved by two or three grains of calomel placed on the tongue, followed, after the lapse of an hour, by a common enema. The calomel may also assist in checking the vomiting.

More difficult to treat are those cases in which diarrhæa is associated with the vomiting. We are deprived of the help of rectal medication and feeding, so long as the purging continues. We must endeavour to control the latter by starch and opium enemata at opportune moments, and by lead and opium suppositories.

Any symptoms of gastric inflammation would suggest, according to Sir A. Garrod, the application of leeches, and internally alkalies, combined with sedatives and hydrocyanic acid. He regards this condition as decidedly rare.

#### THE CARDIO-PULMONARY ATTACKS.

The secondary disturbance of the circulation from which the lung suffers as a result of the cardiac difficulty justifies the use of this joint name, which is also descriptive, the symptoms usually including those of pulmonary congestion and dyspnæa.

There are two forms to the cardiac seizures—the anginal, with predominating pain and dyspnœa, and the syncopal, with prevailing faintness. Both forms are usually complicated with a gastric factor. Indeed, some observers regard the cardiac crises as mainly gastric in origin.

The treatment is in its essentials the same for both forms. Brandy is the immediate indication, and the various methods of stimulation suggested for the relief of the depression of the gastric crises are also called for. In

addition, however, special measures are required in each of the varieties.

In the syncopal attack the following treatment should be applied immediately:

- I. The patient lying quite flat, the foot of the bed or sofa is to be raised so as to cause the head to be slightly lower than the trunk.
- 2. Hot sponges, wrung out of boiling water, should be applied to the nape and to the forehead.
- Heat and friction should be freely used to the extremities, and a warm application placed over the epigastrium.

In the anginal form (which, it must be understood, is not necessarily in this case true angina pectoris, though many cases have been wrongly described as gouty metastasis to the heart which really were of that nature), in addition to the stimulating treatment described, the inhalation of nitrite of amyl is the first indication, and counter-irritation, by means of hot poultices or of a mustard-leaf, should be applied to the præcordial and to the epigastric regions. It is important to administer the stimulants as warm as possible, in order to increase their effect.

Meanwhile, in both cases, the usual indications are to be carried out which have been described at the beginning of this chapter, in the hope that the gouty arthritis may be revived.

#### THE CEREBRAL ATTACKS.

Whether they take the congestive form or the paralytic, these seizures are always the source of great alarm.

The congestive attack, when its dependence upon intracranial hyperæmia is unmistakable, can only be adequately dealt with in one way, by venesection, which is most effectual when practised in the neck. Should there be great objection to this, not fewer than six leeches should be applied to the mastoid region. Five grains of calomel should be placed on the tongue, and a turpentine enema may be administered without delay, and followed, if necessary, in one or two hours by a common injection.

In the paralytic form there may be no evidence of any congestion complicating the paralysis; and in cases in which there is neither rise of temperature nor flush, the question as to the abstraction of blood will be both important to discuss and difficult to settle. Where no major objection is raised, bleeding will probably be of use in producing an alteration in the intracranial circulation, tending either to relieve hyperæmia or to modify the ischæmia to which we have already referred as the more likely condition. Or a via media may be adopted, and leeches applied. In this case also the administration of calomel, and relief of the bowels, are important indications. When these points have been attended to, as well as the general treatment applicable to retrocedent gout, our attitude must be one of expectancy. Time only will decide whether the nature of the seizure is genuinely apoplectic or simply retrocedent. In other cases, however, we may find indications from the first of the relatively benign and purely functional character of the symptoms.

#### CHAPTER XLIX.

# THE TREATMENT OF GOUTINESS AND OF ITS SYMPTOMS.

Goutiness, whether inherited or acquired, may be viewed as potential gout. Its treatment, clearly, must differ from that of actual gout; it is essentially preventive. The hygienic and the dietetic treatment, which will be described further on, belong therefore in a special degree to goutiness. In respect of hygiene and of diet, the treatment of gout is identical with that of goutiness; both affections agree also closely in all those indications which are mainly constitutional.

The subjects of goutiness are liable to the same tendency to acidity and to lithæmia as sufferers from gout. In goutiness, however, the articular symptoms are not to the front, and there is not necessarily always a uratic factor to treat.

The more active treatment of goutiness is directed to the symptoms. These are so multifarious and identified with derangements of such a variety of functions that we can only deal here in broad outline with the most important among them. We propose to consider them in the following groups: The hepatic, the renal, the gastric, the cardiac, the pulmonary, the cutaneous, the neuralgic, and the neurotic. In all these, the gouty factor has to be borne in mind; but in each of them it is some particular function or organ which claims our immediate attention.

#### THE HEPATIC DERANGEMENTS.

In addition to gouty glycosuria and diabetes, which are conveniently classified under this heading, two forms of hepatic disturbance are commonly observed in goutiness—the simple congestive and the biliary form. In neither of these is there any special feature sharply distinguishing the attacks from those occurring in other subjects. The peculiarity resides rather in their marked tendency to recurrence, in the facility with which they are induced by trifling causes, in their resistance to ordinary measures of treatment, and in the relief afforded by those which are directed to the constitutional factor.

Both varieties, but especially the biliary, often present a remarkable neurotic element, the depression being out of proportion with the organic disturbance, and the causation being sometimes almost purely nervous.

The congestive form is more often witnessed at the gouty period of life and in those who may have suffered slightly from manifest gout at an earlier date, and have lapsed into a state of goutiness. Relatively slight departures from a strict diet, or deprivation from the habitual exercise, or any circumstances lowering temporarily the energy, may suffice to originate the congestion. When this is mainly due to some accidental error in diet, and coupled with trivial gastric or intestinal irritation, the treatment by general rest and abstinence from solid food, and by hepatic purges, will afford the necessary relief. In other cases the causation is less obvious, and the customary remedies fail to relieve completely. The first essential in dealing with the affection is a thorough revision of the diet. Wine must be given up; indeed, alcohol in any form may have to be avoided, and a dietary must be devised which shall be absolutely bland and non-irritating.

Such simple medicines as Carlsbad salts taken in hot water every morning, and a mixture containing citrate of potash and nux vomica, will soon lead to improvement, and this will be the more rapid if the patient can be induced to gradually increase the daily amount of exercise. By far the most effectual treatment is a visit to Harrogate or to Carlsbad.

The biliary form is not infrequently witnessed in young subjects who have never suffered from gout, but who inherit a strong gouty tendency. The familiar paroxysmal biliary attacks are often of this nature; they are specially common in the female sex. We need not dwell upon their treatment, since they run a definite course and undergo a spontaneous cure. Our object should be to obviate their recurrence. The other variety, to which males are more liable, is chronic, and apt to be exceedingly obstinate. It is associated with dyspepsia and acidity, and is subject to constant exacerbations variously induced by indigestion, by chill, and by moral influences, the patients being, by constitution and also as a result of invalidism, peculiarly nervous. In both forms we infer, in addition to a catarrhal condition of the biliary mucous membrane, a spasmodic affection of its muscular coat, and we are reminded of the similar affections of the bronchial mucous membrane to which some of the subjects of inherited goutiness are liable from an early age. The management of the chronic ailment is difficult when the advantage of a suitable and protecting climate cannot be secured, exposure to cold winds being almost invariably followed by a recrudescence of the symptoms. The remaining indications have reference to the neurotic tendency, to the dyspepsia, and to the hepatic torpor. Of all these, the most essential is a regulation of the diet such as will restore a healthy nutrition; and a judicious hygiene, which for young subjects

implies more often the precept of rest than that of additional exercise, will aid powerfully towards an improved digestion. The medicinal treatment is that suited to acid and nervous dyspepsia, and to biliary catarrh. Both indications will be effectually fulfilled by a seasonable visit to one of the Continental spas.

We have alluded in previous sections of this work to another form of gouty affection of the liver occurring at a later period of life, and apt to be severe. The neurotic and the spasmodic elements are not here prominent factors. The chief feature seems to be an intimate disturbance of the secreting activity of the hepatic cells, originally induced by a catarrh of the fine biliary ducts. The same general indications as regards diet apply to this affection also. Its early treatment implies rest in bed and careful medication. Gentle hepatic stimulation by 'fractional' doses of mercury, the administration of sodium sulphate and bicarbonate with enough carbonate of ammonium to obviate any depression, and a mild bitter infusion, are the first indications. Warmth is a special requirement; and the hot-air bath administered in bed may be a useful adjunct to other diaphoretic measures. Diuresis will be promoted by a diet at first exclusively of milk. Abdominal and hepatic massage may be resorted to as soon as the hepatic tenderness shall have subsided. A course of sodium salicylate and of chloride of ammonium may now be combined with the sodium bicarbonate. An alternative treatment which can be safely administered with much benefit is the combination of sodium benzoate 20 grains, succus taraxaci I drachm, elixir of orange I drachm, and guaiacum mixture to an ounce; to be taken three or four times in twenty-four hours. In obstinate cases the preparations of iodine and of sulphur might also be thought of. After the onset of convalescence, change to a genial and warm climate should

be arranged, and in due course the hepatic treatment should be cautiously applied at Harrogate or at one of the sulphated sodium mineral springs. Attention to diet will continue to be of primary importance. The question of vegetarianism is one for earnest consideration in these cases.

Gouty glycosuria occurs in every degree and combination. Its presence is always a serious, but usually not an alarming, complication. Under careful management patients often live for many years, sometimes almost wearing out the disease. The renal complication is that most to be dreaded. When the specific gravity of the urine is habitually low in spite of the sugar present in it, we shall suspect renal inadequacy, and additional attention will be needed in the regulation of the nitrogenous supplies. On the other hand, especially in the aged, a slight degree of albuminuria does not of necessity signify damage to the kidney.

The essential part of our treatment concerns diet. Great benefit will accrue from spells of two or three days in bed, at intervals of two or three weeks, or at such intervals as may be indicated, for the express purpose of resting, not only the nervous system, but the liver, kidney, and stomach, by an exclusive milk diet. Prolonged treatment of this kind is not desirable in those of mature years, lest the habit of exercise be lost. Whilst in bed they may with advantage be treated with general massage.

Diet at other times should be of a mixed kind, avoiding excess both in the saccharines and in the nitrogenous supplies. The latter might with great advantage be obtained from vegetable sources, from eggs and from fish rather than from heavy meats, soups, and sauces. Milk should not be taken with meals; but, during their intervals, its use to the extent of  $1\frac{1}{2}$  to 2 pints a day will be most beneficial as a food, as an alkalizer, and as

a means of 'washing out' of the system waste products. Not the least of its functions is to nourish the patient during the night, and also during the longer intervals between meals, and to obviate the necessity for heavy meals, and particularly for heavy meat meals, which are most undesirable. At meals whisky or a little bordeaux are desirable as stomachics.

The medicinal treatment has many aspects. These we can only point out in a general way. The main hepatic indications are: Gentle derivation by the alkaline sulphates, chlorides, and bicarbonates; stimulation by occasional small doses of Plummer's pill or of podophyllin, and by the administration of sodium salicylate (if not contra-indicated), of potassium, sodium, or ammonium benzoate, of guaiacum, of iodine, and perhaps of sulphur. Arsenic has occasionally been prescribed. These remedies will fulfil the additional indication arising from goutiness, which would, however, be most successfully met by a course of treatment at some mineral spring in a favoured climate. The choice of the mineral water is much less important in this affection than that of the physician. The simpler waters will often prove beneficial; but, if the patient be sent to the stronger springs, though greater benefit may be derived, the risks are also greater, and the result will entirely depend upon the judgment and care with which the special treatment and the diet and hygiene may have been regulated by the patient's medical adviser.

Gouty glycosuria and diabetes really call for little medicinal treatment beyond that which belongs to goutiness. In dealing with the latter, we should not lose sight of the fact that in old age the gouty tendency gradually loses strength, and that, meanwhile, the diuresis associated with glycosuria carries out for the patient one of the therapeutic indications.

The bicarbonate and the sulphate of sodium are the medicines suited to the greater number. It is not desirable to render the urine alkaline, and from that point of view the benzoates and the salicylates are preferable to the potassium bicarbonate; but the salicylate is often contraindicated by the presence of albuminuria. In some middle-aged and relatively robust subjects in whom gout takes the leading part, and the glycosuria is slight, more active medication may be wanted, including potassium bicarbonate or citrate, and small doses of colchicum. More often ammonium carbonate, strychnine, and quinine or bark are required at intervals, or should be combined with the sodium bicarbonate.

The *liver* itself does not often provide us with any indications. Any congestion or enlargement would suggest the systematic use of laxatives, and the occasional use of cholagogue remedies; but strong purges are to be deprecated. Mechanical treatment of the liver is less called for than general and abdominal massage. Great benefit is often obtained at mineral springs, and a great part of this is probably due to hygiene and diet. Neuenahr, in Germany, has long enjoyed considerable repute. Of late years Contrexéville and Vittel, in the Vosges, have rapidly risen into popularity.

#### THE TREATMENT OF THE KIDNEY.

A discussion of the treatment of acute and chronic nephritis is unnecessary. In early stages of goutiness the kidney is not organically affected; but it indirectly suffers from results of an imperfect general metabolism, probably analogous to those which Semmola (whose views we quote from Dr. Haig's account of them) regards as the cause of Bright's disease. According to Semmola, this depends, in its first stage, on a diminished formation of urea and

an increased diffusibility of the albumen circulating in the blood. The kidney lesion he would regard as secondary, and as due to local congestion and irritation from a continued passage of a foreign albumen. The albuminuria he considers to be proportional to the blood lesion rather than to the kidney lesion. Semmola attributes the fall in urea formation to the incomplete combustion of certain albumens, owing to failure of function on the part of liver and skin—the skin in particular undergoing, as he shows, considerable atrophy in Bright's disease.

The renal treatment would thus be directed less to the kidneys than through them to the gouty state. It consists mainly of two methods: the treatment by 'flushing,' and the alkaline treatment.

- I. The use of copious draughts of water is a very ancient prescription, too little followed out, or we should hear less of gout. The advantages of this practice are manifold. To the kidney itself it must be of service by clearing the secreting cells of any arrears, by refreshing them, by stimulating their oxidation and metabolism, and thus promoting their nutrition. Excessive flushing may bring with it the risk, pointed out by Sir W. Roberts, of diminishing in the urinary secretion the proportion of chlorides and of pigment, and therefore the solvent power for uric acid. But the mere bulk of fluid which passes through the kidney provides for the solubility of the uric acid within it, and, as pointed out by Roberts, any precipitation which may occur within the bladder is a minor evil compared with the sedimentation of uric acid as sodium urate in the kidneys or in the tissues. Moreover, it is unlikely that any person properly treated in respect of the gout should fail to be safeguarded against the lesser trouble of gravel.
  - 2. The alkaline treatment has already been discussed.

As shown by Sir W. Roberts, the increased alkaline supplies ultimately pass entirely through the kidney. Although these may be quite inadequate to make, as local solvents, an impression upon any peripheral uratic deposits, they must tell upon the kidney for better or for worse. We regard the effect as a favourable one, the tissue reactions being faulty in their tendency to acidity and to imperfect oxidation, for which alkalies are a direct corrective. From the broad standpoint of the theory of renal inadequacy, any remedy tending to improve the condition of the kidney is worthy of consideration; and the general effects of the alkalies, independently of their solvent power for uric acid, are such as to cause them to be recommended for affections of the urinary tract.

The influence of alkalies upon the causes of gout is a matter for separate consideration. Gout may recur under their use, as Sir W. Roberts and others have observed in practice; but it remains a question whether the patient's ultimate condition may not have been much less severe than it otherwise might have been, and whether the kidney may not have escaped, thanks to the method adopted, those destructive changes which are the most dreaded results of gout. The vicarious relief to be afforded to the kidney by action on the skin and bowel, and the direct relief to be secured by an avoidance of all nitrogenous excess and of irritating foods or beverages, are subjects for our further consideration.

#### THE TREATMENT OF URIC ACID GRAVEL.

We have already referred to the occurrence of gravel as an evidence of goutiness, and to the frequency of this symptom in children inheriting the tendency. It should not be understood, however, that this connection invariably obtains. Although gout is associated with an excess of

uric acid, it is important to note that an excess of uric acid, even a considerable excess, is not necessarily gout. As Sir W. Roberts has expressed it, 'all depends upon which side of the kidney the proportion is disturbed.' In gout, the sedimentation originates within the blood district: lithuria, gravel, and stone are identified with a transrenal sedimentation within the urinary district. Sir W. Roberts points out that the urine, once secreted, being practically excluded from vital influences, the fate of its constituents. and of uric acid in particular, is a mere question of chemistry and physics. Uric acid in the urine is clearly a calculable quantity. Not so the circulating uric acid. Part of it, even to-day, is not a calculable quantity; the circumstances of this portion being not only chemical in the usual sense, but, above all, biochemical. Between the two studies there is a wide difference: whilst one can be carried out in the test-tube, the other can be only undertaken with the co-operation of the living cell.

The treatment of gravel, considered in broad outline, should have two objects in view: (1) To increase the solubility of the uric acid, and (2) to decrease the amount of its production if excessive.

- (1) In cases of an increased tendency to precipitation, Sir W. Roberts recommends the administration of alkalies (chiefly at bedtime), the liberal use of salt\* with food, and the free use of vegetables.
- Dr. Vaughan Harley has found piperazine of some service in increasing the solubility, though it takes no effect on the rate of production of uric acid; but its administration was combined with that of bicarbonate of potash, and of iodine.
- (2) To reduce the formation of uric acid, meat and fish should be avoided, as well as alcohol, in favour of non-

<sup>\*</sup> We shall revert to this question under the heading of Diet.

nitrogenous supplies. Dr. Vaughan Harley draws attention to the fact that a quarter of a pound to a pound of sugar may be consumed day by day without any increase taking place in the uric acid excreted. There need not, therefore, be any anxiety as to the use of sugar from the point of view of production of uric acid. According to him, those drugs will be most serviceable which avail to reduce any possible leucocytosis. In this respect quinine and arsenic are invaluable. Exercise is also of great advantage so long as it is moderate.

To these indications should be added the no less important one of free dilution of the urine. A milk diet presents great advantages in this respect.

Lastly, a judicious treatment of the liver on the lines which have been laid down above is a *sine quâ non* in those cases where a gouty tendency is well marked.

It is remarkable that among those *mineral waters* which have been found useful, and are largely recommended, some are included, such as those of Contrexéville and Vittel, in which lime is contained in moderate quantities.\*

In the treatment of gravel, Sir W. Roberts teaches that the secret is to reduce the excessive acidity which, in an immense majority of cases, is the chief cause, and for this we have two methods—diet and medication. 'It is chemically impossible for uric acid to be deposited from an alkaline urine; it may even be said that it is impossible for uric acid to be deposited prematurely—that is to say, within the urinary channels—from a neutral or feeble acid urine. . . . We have in our hands—in principle, at least—

<sup>\*</sup> This is in apparent agreement with the fact pointed out by the writer (in 'The Climates and Baths of Great Britain; being a Report of a Committee of the Royal Medical and Chirurgical Society of London; London, 1895, pp. 271, 273, 274), that chalky Kent suffers a less mortality from calculus than Sussex, Surrey, Middlesex, London, or even than England and Wales.

the absolute power of preventing uric acid gravel.' But since the deposition is lasting, constant watchfulness is requisite, and the changes in the secretion need to be noticed.

The Acid and the Alkaline Tide.—Food, in connection with the treatment of gravel, may be also regarded as medicine. Each of our meals being a dose of alkali, the greater their frequency, the greater also will be the aggregate of hours of an alkaline influence. During the long interval—sometimes as long as fourteen hours—which comprises the night's sleep, the protecting effect of meals is lost, and a dose of alkali is indicated. We are reminded by Sir W. Roberts that the quality and reaction of the urine are constantly varying. The vesical urine represents in some cases the aggregate work of the kidneys for many hours; but it is in the renal urine that the dangerous oscillations take place. The nocturnal urine is of scanty flow, of hyperacid reaction, and of excessive richness in urates. This is the urine that needs correction. 'If we safeguard the night, the day may generally be left to take care of itself.'

Sir W. Roberts therefore recommends that citrate of potash, in doses of from 40 to 60 grains, be taken in 3 or 4 ounces of water at bedtime; 60 grains often render the morning urine alkaline. Bicarbonate of potassium has the same action; that of the acetate of potassium, though more rapid, is less enduring.

As regards the meals, Sir W. Roberts shows that 'at no time during the waking hours does the acidity of the urine tend to rise so high, and its volume to fall so low, as in the latter portion of the interval between the first and second meal in the day; this interval should therefore be abridged.' In connection with afternoon tea, he refers to 'an antacid effect which is too feeble to render the urine

actually alkaline, but which may be quite sufficient to depress its acidity to such a degree as shall postpone the time of precipitation until the urine has escaped from the kidneys, and even from the bladder.'

The Effect of Water in the Mineral Water Treatment.— Whilst recognising that with very great dilution the preventive effect predominates, Sir W. Roberts observes that, by diluting the urine, both the saline and the pigmentary constituents are relatively diminished; and these have been shown to be in themselves protective. It should also be borne in mind that 'in a couple of hours, after even very free potations, the surplus water is entirely removed. Water-drinking has therefore only a limited application in the treatment of lithiasis.'

#### CHAPTER L.

THE TREATMENT OF GOUTINESS AND OF GOUTY AFFECTIONS (Continued).

THE TREATMENT OF THE GOUTY AFFECTIONS OF THE STOMACH AND BOWEL.

GASTRIC CATARRH is one of the most common manifestations of goutiness. Its acute form is exceptional, but the subacute and chronic varieties are of common occurrence.

The subacute attack, especially if sudden and unexplained, should remind us of the possibility of an approaching articular seizure. In this case the treatment would be analogous to that of the metastatic gastric complications, and would include an attempt to localize the inflammation in the foot by pediluvia, poultices, or mustard. Vomiting, if present, will have to be controlled by suitable medication; but for its relief a total cessation of food by the mouth is the first essential, and no drink should be allowed, except perhaps a little ice to suck. Food at this stage not being usually required, rectal alimentation need not be pushed, but a nutrient suppository may be introduced three or four times a day, and if this should be rendered necessary by a continuance of the vomiting, water may be freely supplied by the bowel. The medicinal treatment must be of the soothing and alkaline variety. Effervescing citrate or bicarbonate of potassium may be combined with a little lime-water, and with small

doses of hydrocyanic acid, and of the bimeconate of morphine, which may prove of great benefit in allaying the irritability of the stomach, as well as the patient's discomfort. If the case is placed under treatment early, relief will be rapidly obtained, and in a day or two milk may be borne properly diluted, especially if previously sterilized.

In addition to the alkalies, a specific treatment may be required in some gouty cases, and small doses of colchicum may be combined with the effervescent.

Acid dyspepsia, when coupled with goutiness, is difficult to cure.

Gastric acidity has been credited with a large share in the production of gout. Sydenham held this view: 'The more closely I have thought upon gout, the more have I referred it to indigestion, or to the impaired concoction of matters, both in the parts and in the juices of the body.'

On the other hand, the gouty state itself, and particularly the disturbance of the liver, may react upon the function of the stomach, and perpetuate its failure. We may mitigate the symptoms by introducing alkalies into the stomach, but that treatment will be most effectual which is directed to the liver. Colchicum may be indicated in some cases, and may conveniently be given as a pill; but saline purgatives are a daily essential. We should endeavour to influence the liver by sodium salicylate combined with the sodium and potassium bicarbonates given in effervescence.

Gastric and intestinal antisepsis is of primary importance. For this we have a choice of new remedies, including  $\beta$ -naphthol, benzo-naphthol, salol, and resorcin. The older preparations, such as sodium hypophosphite, sulphur (in tabloids), creasote (in capsules), and mercurial preparations (in pill), will often prove most effectual.

In aggravated cases a short course of nitro-muriatic acid will be necessary as an anti-fermentative and as a hepatic stimulant. Or the patient may be put to bed, and *physiological rest* given to the stomach whilst rectal alimentation is substituted. The return to ordinary food should be made so gradual that the stomach may learn a healthier habit of secretion under the influence of purer blood and of a liver free from congestion.

In this as in all gastro-intestinal gouty disorders, the choice of a suitable health resort is important. Lecorché prefers, in most gastric cases, the mildly calcareous and sulphated mineral springs of Contrexéville, Vittel, Capvern, and Aulus, or, in confirmed and debilitated invalids, the carbonated calcareous springs of Buxton or Pougues, or the mixed carbonated springs of Royat and St. Nectaire. In advanced debility the muriated waters of Cheltenham, Homburg, Kissingen, and Wiesbaden are to be preferred.

Intestinal catarrh is often superadded to gastric catarrh, but it may be a separate manifestation of goutiness, characterized by alternating periods of constipation and of diarrhœa. Gouty diarrhœa is sometimes intractable. Sydenham sought relief from it in artificial diaphoresis when exercise proved ineffectual. Lecorché reports its rapid and permanent cure at Vittel and at Capvern after months of unsuccessful treatment by diet and by bismuth, opium, and other remedies, and he recommends the use of Vittel water, or of Aulus water at meals to patients unable to leave home.

When constipation predominates, and in obstinate cases, the salts or the waters of Carlsbad, Marienbad, or Cheltenham should be resorted to.

Gouty Gastralgia. — The immediate treatment of the attack must be devised on the usual lines. Warmth and

stimulation should be applied to the epigastrium, with laudanum. Sedatives internally, and even the stronger ones, may be necessary at first. Lecorché recommends ether pearls, chloral, and opium, or even subcutaneous injection of morphine. He has not usually found colchicum indispensable, but its administration may be tried with advantage.

It will be well in most cases to begin with such simple remedies as bismuth, sodium bicarbonate and carbonate of magnesia, with hyoscyamus and small doses of hydrocyanic acid, and with chloric ether. Meanwhile counterirritation may be employed. Due attention will be paid to the state of the bowels, which may be relieved by an enema if the administration of a purgative should be undesirable.

Diet will need special consideration in all gastric affections.

### THE TREATMENT OF THE GOUTY PULMONARY AFFECTIONS.

Inherited goutiness is probably responsible for the bronchial, laryngeal, and pharyngeal irritability of many delicate children. A strong neurotic element is the usual accompaniment. A recognition of the gouty feature is essential to a successful management of all these cases.

In the adult it is less likely to be overlooked. Over and above the protective methods, climatic, atmospheric, and general, even more necessary here than in the ordinary affections, special treatment is indispensable. Simple expectorants and inhalations will prove mere palliatives; but the symptoms will yield readily to alkalies, combined if necessary with colchicum, and to the purgative and hepatic treatment, the details of which we need not again mention.

The weaker mineral waters, and in preference the carbonated and the muriated waters, such as those of Ems, Neuenahr, and Soden, are suitable to gouty bronchitic ailments. Harrogate, Eaux Chaudes, Eaux Bonnes, and Cauterets are representatives of the sulphurous springs largely recommended. The treatment by sulphur needs, however, much discretion, and is better adapted to the catarrhal than to the spasmodic forms. Plethoric cases will be benefited by the milder sulphated waters. Temperature, altitude, and surroundings enter largely into the question of selection. A residence in pine forests, at a moderate elevation, is a valuable addition to a mineral course.

Gouty Asthma.—The treatment of this respiratory neurosis resolves itself into that of goutiness, of bronchitis, and of dyspepsia. That the fits of gouty asthma are closely governed by the state of the stomach is attested by practical experience; which on this point sets at rest any theoretical doubt. The asthmatic seizure is preceded either by some mild transgression in diet or by some unforeseen complication in the digestive process, of which the sufferer becomes aware after the event. The dyspeptic prodromata of the attack are realized when it is too late to obviate their culmination in the respiratory crisis. Acidity is a conspicuous feature of the premonitory stage.

These facts point to prophylaxis as the major part of treatment both in view of the threatening attacks, and in a still larger measure in connection with the constitutional tendency, and with the special irritability and delicacy of the mucous membrane of the alimentary and respiratory tracts.

Unfortunately, the memory of some of our worse physical sufferings is proverbially short, especially when they have been more or less self-inflicted. This is certainly the case in asthma and in gout. Painful experiences in the past do not always avail to deter from a relapse into the causes which have led to the painful result. The framing of strict rules of diet is thus of special importance.

The treatment of the attack must be that of ordinary asthma. Upon this we cannot dwell at length. Among the depressants which may be tried, colchicum may occupy a place, but it is not of so much value in this as in some other forms of visceral gout. A rapid purgation, if this should not be contra-indicated, may be of service, in conjunction with remedies which lower arterial tension.

The constitutional gouty factor and the dyspepsia are to be treated during the intervals, which afford us an opportunity of administering such mild tonics as the hepatic delicacy or the idiosyncrasies of the subject may tolerate, together with salicylates, iodide of potassium, and iodine.

If the patient should be resolved to sacrifice everything to the pursuit of health, he will gain much from *climatic treatment*. This will have reference, not only to the respiratory delicacy, but also to that of the alimentary tract. Any southern station would fulfil the main bronchial indication; but it is the exclusive virtue of some places to agree so well with asthmatics as almost to ensure their complete freedom from attacks.

The dry bracing air of altitudes, even during the winter, is beneficial to many of the younger sufferers, and the invigorating effect of a prolonged stay at St. Moritz or at similar stations in Colorado and other regions is of great and lasting advantage.

When the neurosis is grafted on gouty affections of the liver and kidney, or associated with chronic bronchial catarrh, some of the milder mineral springs will have the preference. Mont Dore and some other arseniated waters enjoy in this respect a well-deserved reputation. In some instances, especially in old and debilitated subjects, the safest course will be to trust to the protecting influence of a warm, dry, and equable climate.

# THE TREATMENT OF THE NON-TUBERCULAR AND NON-CARDIAC HÆMOPTYSIS OF GOUTY ELDERLY PERSONS.

Sir Andrew Clark,\* in describing this affection, dwelt upon the importance of adopting a treatment which, although contrary to that suitable to other cases of hæmorrhage, is, in these cases, the only successful one. Absolute rest, careful feeding, ice to the chest, aperients, and strong astringents frequently repeated, were not of the smallest avail in a case which terminated fatally on the fifth day. In another case with analogous treatment, including the administration of lead and gallic acid and the hypodermic injection of ergotine, improvement followed when the patient's fluid supplies were restricted, the ice discontinued, and a mercurial purge ordered, to be followed by an alkaline mixture and ammonia. In concluding a review of other cases of this form of hæmorrhage, which he attributed to minute structural alterations in the terminal bloodvessels of the lung in the absence of any coarse anatomical pulmonary or cardiac lesion, Sir Andrew Clark laid down that it is maintained by frequent and large doses of astringents, and by the amount of fluids which are taken to allay the thirst thus set up; and that the proper treatment consists in 'diet and quiet,' in restricting the use of fluids, and in stilling the cough. Medicinally calomel and salines are the chief remedies; and, for continuous administration, alkalies should be given with iodide of potassium. Sir Andrew Clark also believed in the value of frequently renewed counter-irritation.

<sup>\* &#</sup>x27;Trans. Med. Soc.,' vol. xiii., 1890, p. 9.

# THE TREATMENT OF THE GOUTY CARDIAC AFFECTIONS.

Cardiac failure is usually led up to by renal disease, dilatation gradually supervening in the hypertrophied heart. It is obvious that to restore the hypertrophy, which itself was a product of disease, is more than we can hope to effect. Our treatment must be palliative and protective. The first indication is rest, which tends to equalize the circulation and diminish its tension. diminution of the contents of the vascular system is to be sought for by the careful administration of diuretics, and by as much purgation as is consistent with the patient's strength. The hot-air bath is not available in cases of this kind—at any rate at first. Digitalis as a diuretic, as well as a cardiac tonic, is indicated in some cases. It will be well to seek its highest cardiac benefits by an intermittent use varied with the administration of simpler tonics and diuretics. Other cardiac tonics may also be prescribed, such as strophanthus, convallaria, caffein, strychnine, etc. It is important, as in all cardiac cases, not to prolong the period of absolute rest beyond wise limits. The object was mainly to enable the heart to gradually reduce its capacity and the bulk of its systolic charge. Unless we invigorate it, the next strain thrown upon it will soon reproduce the symptoms, since prolonged muscular inactivity, whilst it wastes the general muscles, also impairs in a definite proportion the muscular strength of the heart.

For this reason passive exercise should be resorted to, preference being given to the resistance movements devised by Dr. Schott; and in suitable cases these may be combined with the use of saline baths.

The intermittent use of mercury as an alterative or as

a hepatic stimulant will be called for in some cases. In other subjects, where cardiac dilatation has been followed by dropsy, Baillie's pill may be cautiously prescribed as probably the best combination available.

In the atheromatous class of cases, vascular degeneracy predominates over that of the kidney. Heart failure is then most commonly due to mechanical circumstances which cannot be rectified. With the progressive attenuation of the coronary blood-supply the heart becomes less and less able to cope with any extraordinary exertion, and it is useless to endeavour to bring it up to that standard. But in selected cases, carefully applied passive exercise may be of value in connection with the general health, and some of the advantage lost by cessation from active exercise may be secured for the liver and other viscera by abdominal massage.

Protection from undue excitement or exertion is the great rule in the management of all cases, and regulation of diet is an important part of the treatment.

# THE TREATMENT OF THE FUNCTIONAL GOUTY HEART.

As pointed out by Dr. Mitchell Bruce, in his valuable paper on the 'Gouty Heart,'\* the existence of goutiness may be long unsuspected, and the patient, frequently too busy to pay much attention to his health, does not become aware of its irregularity until alarmed by symptoms directly referable to the heart; and he often seeks advice less for his constitutional than for his cardiac symptoms. In dealing with such a case, the success of our treatment will depend upon the correctness of our diagnosis. So long as the gouty factor is neglected, purely medicinal cardiac remedies will only make matters worse.

<sup>\*</sup> The Practitioner, January, 1895.

We need not insist upon the principles of constitutional treatment applicable to this as well as to other cases of goutiness. The immediate requirement is relief to the cardiac symptoms, which are those of weakness and irritability, viz., inequality to any sudden strain, angina-like seizures brought about either by exertion or by indigestion, giddiness and faintness, insomnia with palpitation, irregular pulse, and fluttering at the heart.

The heart being clearly overdriven, the first requisite is rest. Recumbency is, next to sleep, the best, and, when associated with sleep, the highest, form of rest to the heart; and if this be combined with a light and nutritious diet, which taxes neither the stomach nor the liver, much advantage will be gained without delay.

Most patients with cardiac attacks of some standing are dependent for relief on the use of nitrite of amyl and nitroglycerine. A few days' rest in bed on light food or exclusive milk diet will put a stop to the anginal trouble, and break through the drug habit. A better opportunity will arise of treating thenceforth the cause of the affection instead of its symptoms.

Where goutiness is pronounced, iodide of potassium will fulfil a constitutional as well as a cardiac indication, and the hepatic treatment which has been described will find its application.

Cardiac tonics are not contra-indicated, so long as the absence of high tension of pulse identifies the case as one of purely functional angina. Small doses of digitalis or strophanthus and strychnine will be of service in reducing the curable dilatation, which generally underlies the symptoms. Their use should, however, be temporary, and it loses importance with the progress of the hygienic measures.

The real cure of the 'functional gouty heart,' as of gout

itself, is exercise; and the preliminary measures described are the early steps in that method. Passive movements may be begun even on a milk diet. When solid food is resumed, a heart free from valvular defect can quickly be trained to efficiency by Schott's resistance exercises. The next stage is active muscular work in the open air, gradually increased from mere level walks to walking uphill, to golfing, horse-exercise, cycling, and even tennis.

On these lines the average case can be got well at home, but spas may be visited with great advantage in this country and abroad. Under careful local advice, Buxton, Leamington, Llandrindod, or even Harrogate, may prove most beneficial; and at Nauheim special treatment will be applied on the basis of a large experience.

The happy result of a well-managed treatment of the cardiac neurosis is often a permanent cure of the goutiness which led to it.

#### THE TREATMENT OF THE GOUTY NEURALGIÆ.

The severity and duration of many neuralgiæ is due to their treatment being too often merely symptomatic. Anodynes alone will not cure them if they are due to a goutiness which is overlooked or neglected. Constitutional treatment must begin with diet; appropriate medication can then take effect, and hygiene will complete the cure.

The complete success of the mineral-water treatment in cases which had long proved rebellious is due to the application of these broad principles. Balnear treatment is not, however, the only successful method; moreover, its application also requires great judgment. Excellent results are to be obtained without mineral baths, but only after a due appreciation of the special requirements.

The goutiness of neuralgic patients cannot be treated on general lines. They are jaded by prolonged pain, worn out by insomnia, and debilitated by imperfect alimentation. Any depressing influence can only add to the trouble. Neither excessive purgation nor an alkaline medication is admissible. The first indication is sleep, and this must be secured by efficient narcotic doses. Light and nourishing food will then supply a growing fund of strength, but the diet must be planned with due regard to the gouty state.

The most efficient medicines are those which least depress, whilst correcting the constitutional fault. Bicarbonate of sodium is available in moderate doses, and may be combined with sodium salicylate. The most useful remedy is a combination of the latter with iodide of potassium and with guaiacum, and the effect is much raised by the addition of a sufficient dose (at least 10 minims) of the tincture of iodine. The relief afforded is usually such as to be gratefully acknowledged by the patient.

This treatment has been found markedly beneficial in obstinate trifacial neuralgia, with the further addition of half-drachm or drachm doses of perchloride of mercury solution. General massage is an important adjunct to the dietetic and medicinal treatment, which should be followed by the tonic influence of change of air.

In neuralgiæ of the large nerves, and particularly in sciatica, medicinal treatment should be supplemented by the hot-air bath, followed by gentle massage of the painful part. In these affections the thermal springs of Bath, Aix-les-Bains, Aix-la-Chapelle, Néris, Plombières, Ragatz, Gastein, Wildbad, etc., are of undoubted service. The milder calcareous sulphated waters mentioned above are also recommended by Lecorché. The sulphurous waters of Harrogate are of acknowledged utility. A great part of the benefit derived at all thermal stations is doubtless due to the combination of massage with the heat of the

douche. Sulphur also has a beneficial effect internally, though its virtues cannot compare with those of iodine.

The treatment of gouty myalgiæ agrees almost in every point with that of gouty sciatica, and does not need separate description.

### THE TREATMENT OF THE REMAINING GOUTY AFFECTIONS.

In this brief sketch of the treatment of goutiness and of its manifestations, many affections have not been included. Various gouty neuroses, and the gouty disorders of the organs of special sense, of the larynx and pharynx, and of the skin, have not been dealt with. In all of them the gouty factor has to be regarded, and its appropriate treatment, which has been detailed, goes far towards a cure of the local trouble; but a full account of the individual treatment of each affection would be a task out of proportion with the space at our disposal.

#### THE MEDICINAL SPRINGS.

#### CHAPTER LI.

# THE TREATMENT OF GOUT AND GOUTINESS BY MINERAL WATERS.

#### THE MEDICINAL SPRINGS.

THE growing practice of sending gouty patients to undergo a course of treatment at various watering-places is encouraged by fashion, but it is, beyond any doubt, founded upon the solid basis of clinical results. The patients themselves are aware of the benefit they derive, and willingly submit to the discomfort entailed.

The popularity and efficacy of this form of treatment, and the great variety in the composition of the different waters, render indispensable a cursory review of the whole subject, and some account of the various springs which are suitable to the several phases and kinds of the gouty affections.

The General Characters and Chief Varieties of Medicinal Springs.—In gouty arthritis the most obvious indication is the external and local application of the treatment; in visceral gout and in goutiness the internal use of the waters is the most essential. On the other hand, the constitutional

aspect of arthritic gout demands internal medication, and visceral gout and goutiness are also largely dependent for their improvement upon the effect of the baths upon the general cutaneous surface. It follows that the best, it might almost be said the only, springs available are those suited for external as well as for internal use; and since cold applications are eminently contra-indicated in gout, our choice is limited to the *thermal* springs. An appreciation of this fact has led to the artificial heating, for external use, of various waters, the medicinal value of which is great, but which by reason of their low temperature would not have been available for the adequate treatment of gout. The most striking instance in this country is that of Harrogate.

Again, a sufficient heat being, for external application, far more important than the solids contained in solution, whilst pure water imbibed in sufficient amount is a valuable therapeutic agent, various neutral or indifferent springs containing relatively small quantities of solids are turned to account by reason of their thermality. These simple waters we shall include in Group I.\* Bath, Buxton, Wildbad, Gastein, Ragatz-Pfäfers, Schlangenbad, and many other 'Wildbäder,' belong to this group. To this class also belongs Hammam R'Ihra, a mildly saline hot-water spring (II4° Fahr.), situated about 75 miles from Algiers, at an elevation of 2,000 feet above the sea-level, in a site unexcelled in its beauty and salubrity.

The most important mineral constituents of the active springs may be classified as the alkaline carbonates and the earthy carbonates; the alkaline sulphates and the earthy sulphates; the chlorides of the alkalies (but chiefly of sodium) and of the earths; the sulphides and sulphuretted

<sup>\*</sup> The grouping which is here suggested is slightly altered from Dr. Burney Yeo's excellent classification of the mineral springs.

hydrogen; and the small quantities of *iodides*, *bromides* (Woodhall Spa), and *arseniates*, and of the salts of *lithium*, which occur in various springs. Lastly, free *carbonic acid* is given off by many of them.

For convenience we refer to the various waters as carbonated, sulphated, muriated, chalybeate (or containing iron), and sulphurous. None of them, however, are pure solutions of any of these substances; these abbreviated expressions merely imply a preponderance of the constituents to which they refer. All analyses show a more or less mixed composition of the waters.

viz., sodium chloride in abundance, and traces only of the other alkaline salts, but often much carbonic acid gas, which usually keeps some carbonate of lime in solution. (Cold or tepid, gaseous springs: Homburg, Kissingen, Leamington; hot, non-gaseous: Wiesbaden, Baden-Baden; hot, gaseous: Nauheim, Rehme, Bourbonne-les-Bains, etc.)

Brine baths (Droitwich, Kreuznach, Ischl, Rheinfelden, Aussee, Reichenhall, Harzburg, and many others) are not in general as suitable in gout as in many other affections, although the local effect on stiffened articulations, or in chronic sciatica, may be beneficial.

The alkaline springs contain sodium bicarbonate largely, with an excess of carbonic acid gas, and only unimportant percentages of the other alkaline carbonates. Other salts may be present in insignificant amounts. The springs may then be described as simple alkaline, forming our Group III.

The strongest alkaline springs, those of Vals and Vichy (5 to 6 pro mille), do not contain sufficient carbonate of lime (0.46 to 0.57 pro mille) to counteract their efficiency in vesical and prostatic catarrhs, and in biliary and urinary concretions; but their chief use is in gout, for which some

of these springs possess the desirable temperature. Neuenahr (famed for diabetes, a much weaker alkaline spring) is also thermal, a property lacked by the other German alkaline springs, which include Fachingen, Bilin, Salzbrunn, and Assmannshausen. The lithium bicarbonate reaches in the last-named its highest recorded proportion (0.027 pro mille); but the Bonifaciusbrunnen of Salzschlirf (belonging to Group II.) contains the highest known percentage of lithium as a chloride (0.218 pro mille), with 10.2 pro mille of sodium chloride.

Group IV. is formed by the alkaline muriated springs, of which Ems is the type, containing with sodium chloride varying amounts of sodium bicarbonate; they are well adapted for the treatment of respiratory and gastric catarrhs. The Royat and La Bourboule waters present the advantage of a little arsenic in addition to traces of lithium.

Group V., that of the alkaline sulphated springs, occupies a large place in the treatment of gout and of goutiness. Combining the neutralizing and alterative properties of sodium bicarbonate with the laxative and eliminative action of the sulphate of that metal, their power for good is great, but it calls for a corresponding amount of discretion in its application. The members of this group are not numerous, but they differ much in their strength. Carlsbad, with its sixteen springs, varying in temperature from 95° to 160° Fahr. (Sprudel), heads the list, and is practically unrivalled. Brides-les-Bains, which has been described as 'the French Carlsbad,' is less searching, but applicable to the same class of cases. Marienbad enjoys a wide reputation for the treatment of obesity. Its waters are not naturally thermal, ranging from 9° to 11° C., but their internal effect is similar to that of the Carlsbad springs. It enjoys a greater elevation (628 metres above the sea-level), and a bracing climate.

Tarasp, in the Lower Engadine, is at a much greater elevation (1,200 to 1,270 metres above the sea-level). The Lucius spring contains 14.7 total solids in 1,000 parts (bicarbonate of sodium, 4.9; chloride of sodium, 3.6; sodium sulphate, 2.1; and carbonic acid gas, 2,380 c.cm.). Numerous chalybeate springs occur in the vicinity.

Group VI.—The alkaline earthy springs contain chiefly lime and magnesia in the shape of sulphates and carbonates, with small and varying amounts of other metallic salts, usually in association with free nitrogen and carbonic acid gas. They have been found of use in catarrhal states of the mucous membranes, and particularly of the urinary passages, and prostate, and in renal and vesical concretions.

Their suitability in gouty affections is to be gauged by the relative amount of sodium and magnesium sulphate which some of them contain, in addition to the carbonates. Contrexéville, Vittel, Martigny, Capvern, Evian, Wildungen, and Driburg are the best known representatives of this group. Cheltenham waters contain a larger proportion of sodium and magnesium sulphates than any of these.

Group VII. is one of the most important, including the hot and the cold sulphur springs: Aix-les-Bains and Aix-la-Chapelle, Baden near Vienna, Baden near Zürich, Schintznach (33° C.), Helouan, near Cairo (32° C.); Uriage; Allevard; St. Honoré; and in the Pyrenees Cauterets, Eaux Bonnes, Eaux Chaudes, Barèges, Bagnères de Luchon, St. Sauveur, and Amélie-les-Bains; and lastly Panticosa in Spain, and Mehadia in Hungary, are all thermal springs.

Eilsen, Nenndorf, Meinberg; Schimberg, Gurnigel and Heustrich, at moderate elevations in the Swiss Alps; Weilbach, in the Taunus range near Wiesbaden; Enghien, near Paris, and Challes, near Aix-les-Bains, are cool sulphur springs.

To the same class belong, in this country, Harrogate, Dinsdale - on - Tees, Moffat, Strathpeffer, Llandrindod, Builth; and in Ireland, Lisdoonvarna.

Group VIII.—The chalybeate springs, according to Dr. Hermann Weber's classification, may be: (1) comparatively pure, with only feeble quantities of any other substances in solution, as those of Tunbridge Wells, of one of the springs at Harrogate, of Flitwick, Spa, Schwalbach, and others; (2) of mixed composition, either containing carbonates and sulphates of sodium, calcium, and magnesium and common salt, as those of Orezza, Pyrmont, Driburg, St. Moritz, Bussang; or containing sulphate of iron, as the waters of Flitwick, Muskau, Parad, Alexisbad, and Ratzes. Those of Roncegno and Levico, in the Austrian Tyrol, are powerful, and contain sulphate of iron in conjunction with arsenic (H. Weber).

# THE MINERAL SPRINGS OF THE NORTH AMERICAN CONTINENT.

The following particulars are supplied by Lyman:\*

The thermal waters of Arkansas hot springs contain little earthy or saline matter. The hot springs in South Dakota are rich in chlorides and other salts.

In the United States, purely alkaline waters are few and of low strength; e.g., Bladen springs in Alabama, the Congress and the Seltzer springs in California, the latter containing as much as 10 grains in the pint of magnesium carbonate (H. Weber), the St. Louis springs in Michigan, and the Sheldon springs in Vermont, are the best known.

The Canadian springs of St. Katharine and Caledonia, the wells at St. Clair, at Mount Clements, and others in

<sup>\* &#</sup>x27;Twentieth Century Practice: an International Encyclopædia of Modern Medical Science,' etc. Edited by T. L. Stedman, M.D., New York City, vol. ii., 'Nutritive Disorders,' 1895.

Michigan, the Saratoga springs in New York, and the Crab Orchard springs in Kentucky, represent the sulphated saline group. To these may be added the Estrill springs, the Bedford springs, and the Midland well (H. Weber).

The muriated saline group includes the Glenwood springs in Colorado, the St. Catherine wells, the Michigan Congress spring, the Spring Lake well, the Fruit Port well, the Saratoga springs, and the Ballston Spa (H. Weber).

The feebly mineralized waters of Poland, in Maine, and of Wakusha, in Wisconsin, approximate those of Contrexéville and Vittel, and are suitable for cases of diabetes and of renal, vesical, or biliary concretions.

According to Dr. H. Weber, the mixed chalybeate springs in North America are: the Bailey springs, the Stafford springs, the Greencastle springs, the Estrill springs, the Schooley Mountain springs, the Montvale springs, and the Rawley springs.

The sulphate of iron springs are: The Oak Orchard acid springs, the Bath alum springs, and the Variety springs.

Lyman gives an interesting quotation from Beaumont Small's\* classification of the mineral springs of the United States: Small refers to the waters found in the Western mountainous district, extending from the Pacific coast almost to the Mississippi River, as 'chiefly alkaline springs containing a few grains of the purgative salines, generally of a high temperature and strongly sulphurated. Thermal saline springs, with or without sulphuretted hydrogen, also occur, such as the Utah and Kalistoga springs.

'In the East the highly-carbonated and alkaline-saline springs are the most common. The only thermal springs are in Virginia and the South. These are only slightly sulphurated, and almost imperceptibly alkaline.

<sup>\* &#</sup>x27;Reference Handbook of the Medical Sciences,' vol. lv., p. 694.

'In the great Palæozoic Basin, which formed the bed of the early sea, we only find the waters rich in salines. Those containing chlorides are to be found everywhere, but such as contain the purgative sulphates are chiefly confined to certain districts, as in Kentucky, Michigan, and western New York. In these the active salt is sulphate of magnesium. In this they differ from the purgative waters of the West, which owe their properties to sulphate of soda.

'In Canada the springs are chiefly saline and alkalinesaline; a large proportion are ferrated and sulphurated.'

#### THE HOT SPRINGS OF NEW ZEALAND.

The writer is indebted to Dr. W. E. Collins, of Wellington, for valuable information concerning the therapeutic uses of the celebrated thermal springs of the Hot Lake district in the North Island, which covers an area fifty miles in length and twenty miles in width, and in which Rotorua 'with its numerous hot springs, its geysers and mud volcanoes, its green, yellow, and blue lakes, and its terraces of silica,' is the centre of attraction.

The Government have established a hospital for the balnear treatment of patients.

'The mineral waters of this district are classified from analyses made in the Colonial Laboratory under the following groups:

- 1. Saline, containing NaCl.
- 2. Alkaline, containing carbonates and bicarbonates of soda and potash.
- 3. Alkaline silicious, containing much silicic acid, but changing rapidly on exposure to the atmosphere, and becoming alkaline; these on cooling deposit silica, and so form the terraces.

- 4. Sulphurous, containing sulphuretted hydrogen and sulphurous acid.
- 5. Acid, containing an excess of mineral acids, such as hydrochloric and sulphuric acids.
- Muddy waters; mineral waters are here mixed with a pasty clay. It is an acid mixture, rich in sulphuretted hydrogen.'

#### 'The chief medicinal baths are:

- 1. The Priest's Bath, Te Pupunitanga.
- 2. Madame Rachel's Bath, Whangapipiro, cooled to any temperature.
- 3. The Painkiller Bath.
- 4. The Coffee-pot Bath.
- 5. Hinemaru or Stonewall Jackson's Bath.
- 6. The Blue Bath, a warm swimming-bath.
- 7. Cameron's Bath.'

The following analysis of the cold effervescing water of Puriri (about 10 miles distant from Grahamstown), shows that it is analogous to the waters of Fachingen and Ems.

#### THE PURIRI WATER.

				Gra	ins per Gallon.
Chloride of sodium	-	-	-	-	21.938
Iodide of magnesiu	ım -	-	-	-	Traces
Sulphate of soda	-		-	-	0'940
" potash	-			-	4.938
Carbonate of iron	-	-	-	-	Traces
Bicarbonate of lime	e -	-	-	-	28.506
" maj	gnesia	-	-	-	25.625
" sod	a -	-	-	-	452'393
" lith	ia -	-	-	-	Traces
Silica	-	-	-	-	2.772
Phosphoric acid -	-		- N	ot dete	ermined

Dr. Collins writes: 'I have found the Puriri water most useful in gout. I know of one instance where a gentleman had had for many years at least one, often two, attacks of gout during the course of each year, and was thereby incapacitated from work for longer or shorter periods of time. He had had all kinds of treatment from many different practitioners, but for some years now he has not suffered at all, and he attributes his freedom from gout during that time to the fact that he drinks his water daily; the only other treatment he adopts is that of having a Turkish bath once or twice a week.'

To the favoured few to whom time and distance are no obstacle in the pursuit of health, the New Zealand springs might offer the great advantage of a thorough course of thermal treatment during our winter months, when this is not attainable under favourable climatic conditions in the Northern Hemisphere.

#### CHAPTER LII.

## THE USES AND THE SELECTION OF MEDICINAL SPRINGS.

#### THE SULPHATED WATERS.

THE GENERAL THERAPEUTICAL ADVANTAGES OF SPAS.

Theoretically the choice is perplexing, but happily our practical selection is guided by the results. We are struck by the large measure of success reported almost uniformly from the various baths, the effects of which, as gauged by analysis, should present the strongest contrast. Allowance should be made for an influence of the *genius loci*, which turns patients into advocates for the resort with which they are identified; yet we cannot avoid the conclusion that solid advantages belong in common to the majority of health resorts, and that their health value is not to be reckoned in grains of salt per gallon of the mineral waters, nor according to any chemical formulæ.

Almost every variety of mineral water can now be obtained and used by patients at their own homes; but the relative inefficiency of this form of treatment shows that the benefit derived at watering-places is not altogether due to the daily consumption of so many glasses of this or of that mineral water. Complete rest from the fatigue and anxieties of business, and from the routine of

home-life, the novelty of the surroundings, the change of air and of scenery, the longer hours spent in the open air, the altered and specially-selected dietary, the increased amount of exercise, the regular and early hours—these are some of the advantages which are common to all resorts, but which go to establish the individual reputation of each.

There is also the exhilarating effect of the amusements now provided at most Continental resorts, and the importance of which is beginning to be appreciated at our own spas.

Medical reasons also explain the prevailing average of favourable results. Mutual criticism has advanced the local physicians' knowledge of the shortcomings of each mineral spring, as well as of its virtues, and has led more and more to the avoidance or to the correction of the former. Much improvement has resulted also from a wider appreciation of the great principles of balnear treatment: their application is now more varied, according to requirements, and more judiciously adapted to each individual case. Lastly, another element in producing this uniformity has been the efficiency and the more and more widespread adoption of the Aix method. So important are its results in gout that they probably in great measure dwarf chemical and therapeutical differences, which otherwise might have been more prominent.

Summer is the best, and at some stations the only, season for a visit to the springs. In winter some of the most efficacious spas are deserted, and at those which remain open in Great Britain and on the Continent the atmospheric conditions are not those to be desired for the most successful management of gout. This circumstance gives special value to the thermal springs of subtropical zones, and to those of the Antipodes.

#### THE GENERAL INDICATIONS.

The various types of gouty affections give different indications as to the internal or external use of the waters.

- I. A separate class is that of the late results of chronic gouty arthritis, the thickened and stiffened articular structures. For these local treatment is the essential, though not the only, requisite.
- 2. In the other form of advanced local changes, the *tophaceous*, the internal treatment assumes greater importance by the side of the local.
- 3. Cases of relapsing acute gout, of a sthenic kind, need a full measure of constitutional treatment.
- 4. The milder cases of liability to slight and infrequent attacks of acute arthritis need not be separated from those of general goutiness in which articular manifestations are ill developed. In all these, constitutional treatment is needed, and should be aided by balnear treatment. In inherited goutiness prophylaxis is the early indication.
- 5. Gouty glycosuria and renal disease are sharply defined from other groups. Their treatment is largely dietetic as well as constitutional.
- 6. The remaining group, that of the abarticular visceral or peripheral manifestations of goutiness, includes: (a) The affections of the skin and its appendages; (b) the affections of the mucous membranes, respiratory, gastric, and intestinal; (c) the affections of the liver and biliary system; (d) the renal and vesical affections. Internal treatment is needed in all, and external treatment is of use, but the indications vary with the structures involved.

The skilled and cautious external application of the thermal waters is beneficial in almost all cases of chronic articular gout; and in the majority of the visceral forms of goutiness their value is great. The contra-indications are:

acute cutaneous complications, cardio-vascular degenerations, and advanced age. Safest and most generally successful are the thermal baths, such as those at Bath, Buxton, Aix-les-Bains, and many others, which are only slightly mineralized. A high percentage of salt or of sulphur may prove too exciting in some cases. Brine baths are for this reason less indicated in gout than in rheumatism, and in gouty skin affections they are contraindicated.

Internal treatment is a much more difficult question. A few indications are simple and direct: Iron and arsenic for anæmia; sulphur for some chronic gouty affections of the skin; sulphur for catarrhal affections of the respiratory, gastric, and intestinal mucous membranes; and, again, sulphur for hepatic torpidity. Beyond this, opinions are at variance and conclusions are doubtful. For instance, the desirability of treating a nervous case by the arsenical constituents of a given spring should not close our eyes to the disadvantages which may be associated with this gain, nor to preponderating advantages which might elsewhere be secured. After all, a minute quantity of arsenic added to any mineral water might fulfil this relatively insignificant part of the mineral cure. To the arbitrary modification of mineral waters deficient in some desired constituent, we shall presently refer.

More debatable are the indications for the alkaline, the sulphated, the muriated, and the calcareous waters. It is easy to lay down hard and fast lines: the alkaline carbonates should suit all cases of excessive acidity; the alkaline and magnesian sulphates are the proper treatment for hepatic engorgement and constipation; a similar influence, without so much purgative effect, should be found in the muriated springs; the milder calcareous waters should allay the irritability and clear the obstruc-

tions of catarrhs, and particularly those of the alimentary canal. Matters, however, are much complicated by the presence in most springs of a variety of salts, sometimes almost contradictory in their action, and we are compelled to inquire more closely into the effects of individual spas.

#### THE SULPHATED WATERS.

We may deal first with the relatively simple question as to the use of sulphated waters, such as those of Carlsbad, Marienbad, Brides-les-Bains, etc. There is little doubt that these are in principle applicable to a large class of cases; the question as to their use is rather one of degree and of adjustment. It is sometimes alleged that their effect is depressing. This, however, is not borne out by the testimony of experienced physicians; it may have arisen in connection with their injudicious use by the patients.

Idiosyncrasy should be borne in mind in this as in all other matters relating to gout. In some cases the question may lie between the relative suitability of the sulphatic treatment and that of the derivative and laxative treatment obtainable at the sulphurous springs, and at some of the calcareous springs respectively.

The value of the muriated and of the calcareous springs has often been questioned; and a yet more serious question relates to the action of the sodic springs in gout. Sodium being the chief constituent of all alkaline and of all muriated springs, this doubt concerns a very large proportion of the most highly reputed mineral waters. To these more disputed points in practical balneology we shall now give our attention.

#### CHAPTER LIII.

## THE USES AND SELECTION OF MEDICINAL SPRINGS (Continued).

#### THE CALCAREOUS WATERS.

LIME as sulphate or carbonate is a widespread constituent of drinking-water. Hard water has sometimes been accused\* of producing gout or of favouring its manifestations. In the tables of mortality collated by the writer in the Climatological Report of a Committee of the Royal Medical and Chirurgical Society, † it is shown that, in spite of the calcareous nature of its water, Kent suffers less severely from gout than Sussex, and much less severely than Surrey or Middlesex, although its mortality from gout is greater than that recorded in London, and much greater than that belonging to England and Wales. It is noteworthy that, in their mortality from rheumatism also, Kent, Sussex, and Surrey preserve the same order, and that in both cases Kent yields almost the same returns as London. Middlesex, which suffers more than the three other counties in connection with gout, suffers less than any of them in connection with rheumatism. The figures extracted from the Registrar-General's annual report for 1891 are as follows:

<sup>\*</sup> Cf. Duckworth (loc. cit., pp. 361, 412). † Loc. cit., p. 272.

#### MORTALITY PER MILLION PERSONS LIVING.

Gout.	Rheumatism.			
England and Wales - 22'45	Middlesex - 27.55			
London 36.24	London 28'42			
Kent - 38'32	Kent - 28:43			
Sussex - 55'74	England and Wales - 36.69			
Surrey - 60.85	Sussex - 37.76			
Middlesex - 63'72	Surrey - 43°47			

#### Calculus.

Kent	-	-	+	-	7.41	
England	and	Wa	les	-	-	8.14
Sussex	-	-	-	-	8.99	
Surrey	- "	-	-	-	10.43	
Middlese	ex	-		-	12'05	
London	-	-	-	-	-	14'21

The last table shows a perceptibly lower rate of mortality from calculus in Kent as compared with England and Wales, and especially with Sussex, Surrey, Middlesex, and London. This remarkable fact almost disposes of the notion that calcareous water favours the formation of stone. Indeed, lime-water and the salts of lime were formerly prescribed as specifics not only for stone, but for gout; and at the present time the waters of Contrexéville and Vittel, in spite of the salts of lime which they contain, are recommended for urinary concretions almost in preference to those of Vichy, which contain relatively less calcium.

The behaviour of the salts of lime towards the tissues is still incompletely understood. In some diseases, such as rickets and osteo-malacia, calcium is imperfectly fixed by tissues in spite of an abundant supply; whilst in atheroma and in other calcifying diseases they attract and detain it, although no excess of lime may have been ingested. The fault seems to lie rather with the tissues than with the

supply, which, with an average dietary, is more than sufficient for the needs of the economy. In short, there is always a surplus passing out through the kidneys and bowel; and so long as this habitual surplus is not drawn upon for the pathological purpose of deposition, no harm will come of its being increased by the ingestion of calcareous waters, provided the urinary and alvine excretion is promoted rather than checked by them, and provided also the percentage of lime is not such as to act as an irritant to the mucous membrane of the stomach.

The belief in a solvent power of carbonated calcareous waters for uric acid has received some confirmation from the comparative observations of Fürst\* on the behaviour of urines secreted after drinking the various mineral waters. The method employed, which is open to obvious objections, consisted in adding (under the same experimental conditions) to 200 cc. of each urine o's gramme of dried uric acid, and subsequently filtering and weighing after digesting for twenty minutes at 37° C. A urine which spontaneously deposited uric acid also deposited uric acid when passed after draughts of Assmannshausen, Wiesbaden, and Salzschlirf waters. Fachingen, Vichy, and Wildungen waters caused, on the contrary, part of the added uric acid to be taken up by the urine, Fachingen water being the most effectual in this respect. Fürst arrives at the conclusion that the solvent power of springs depends upon the total amount of carbonated bases they contain, and that calcium bicarbonate and potassium bicarbonate are as effectual as the sodium salt.

The virtue of the milder calcareous mineral springs is probably due to their harmlessness, which permits considerable libations to be indulged in. If, as often occurs, they should contain feeble proportions of diuretic, laxative,

<sup>\*</sup> Deutsche Medizinal Zeitung, January, 1893 (quoted by Levison).

ferruginous, or alterative salts, these salts acquire progressive activity in proportion to the bulk of the fluid ingested, and, owing to their great dilution, their action is combined with a minimum of irritation.

The Special Indications.—Dr. Galland-Gleize, in an interesting monograph on 'The Mineral Waters of Vittel,' and these may be taken as a fair sample of the group of bicarbonated and sulphated calcic waters, dwells upon their eupeptic, diuretic, laxative, and cholagogue effects, and claims for them a stimulating action on general metabolism and a depurative action for uric acid, the excretion as well as the production of which are ultimately reduced. He finds them well suited for all forms and phases of gout, and specially suited for the visceral complications of goutiness, whether gastric, renal, hepatic, or glycosuric, and for biliary and urinary lithiasis. In vesical and prostatic catarrh they are also of much value.

The diuretic, laxative, and cholagogue action is sufficiently explained by the presence of sulphate of sodium and of magnesium;\* the eupeptic action not only by these, but probably by the sedative action of carbonic acid gas, and by the calcium carbonate and sulphate. Two to eight glasses are to be drunk fasting at short intervals in the morning, and one to three glasses four hours after lunch. He warns against the excessive amounts sometimes taken by patients. The individual allowance should be carefully regulated by the physician.

<sup>\*</sup> Dr. Galland-Gleize claims for the water of Vittel that it is relatively more magnesian and less calcareous than that of Contrexéville, and therefore more purgative and also more digestible.

#### CHAPTER LIV.

## THE USES AND SELECTION OF MEDICINAL SPRINGS (Continued).

#### THE MURIATED WATERS.

GENERAL INDICATIONS.—The value of sodium chloride springs in gout is a much vexed question. Of their value in various other affections no doubt can be entertained. As in the case of lime, the diluted solutions of sodium chloride can be taken in large quantities, and, aided by the bulk of water, the special activities of the salt come into play.

- I. Foremost among the therapeutic properties of sodium chloride is its diffusibility, which enables it to visit every part of the body. Substances, and in particular urea, with which, according to some physiologists, soluble combinations or double salts are formed, may by this means be more readily washed out of the tissues and excreted.
- 2. Probably, by facilitating and accelerating the circulation of the juices, it *promotes metabolism*, and lessens the tendency to various *concretions*.
- 3. It promotes appetite as a stimulant to the sense of taste, and as a stimulant to the gastric mucous membrane.
- 4. It supplies the stomach with the hydrochloric acid, and the liver with the sodium, which they need for their respective secretions. It is therefore a digestive and hepatic stimulant.

Among its peptic properties, Stadelmann has pointed out its power of increasing the tolerance of the stomach for large doses of sodium bicarbonate, as much as 20 or 30 grammes of which have been taken *per diem* in diluted solutions of sodium chloride and of carbonic acid gas.

Dr. Hermann Weber dwells on the influence which it exerts upon metabolism, through the secreting apparatus of the bowel and through the portal system, and holds that it quickens tissue-change, and thus 'promotes the absorption of pathological products without lowering the organism. In larger doses, however, beyond about 5 drachms per diem, irritation of the mucous membrane of the stomach and intestines may be produced.'

In most of the muriated springs the effects are modified by the presence of carbonic acid, which acts as a sedative on the nerves of the stomach, whilst stimulating the secretion and the peristalsis. It may, of course, produce temporary dilatation. More commonly, any excess is absorbed or dispelled.

Other salts often occur in small proportions in the muriated springs, and their properties will have to be taken into account.

The Muriated Baths.—Considerable attention has of late been directed to the specific effects upon the heart of the hot springs of Nauheim, which contain an abundance of carbonic acid gas in addition to sodium and calcium chloride. This subject is not foreign to gout, some of the visceral complications of which are cardiac. Moreover, the cardiac effect of the baths is held to be largely due to a general influence on the metabolism. Absorption of the salt through the skin probably does not take place. Neither is it likely that any considerable amount of water should be drawn from the body by the strong saline bath.

There is, however, little doubt that the combined action of the salt and of the carbonic acid stimulates the nerve endings and capillaries of the skin, and through them the nerve centres, and, in a reflex way, the entire organism.

The Special Indications.—The debility of convalescence, of most forms of anæmia, and especially of chronic dyspepsia, or of chronic hepatic inadequacy or congestion, is the indication specially applicable to the group of gouty ailments, although many other conditions foreign to gout are benefited.

Among gouty cases, those are held to be specially suited for this treatment which do not present the indications for the more searching saline mineral springs. Thus, according to Dr. Hermann Weber, 'the muriated alkaline waters of Royat, Ems, or Baden-Baden are suited to the more delicate constitutions; and for lean and weak gouty subjects the simple muriated springs of Homburg, Kissingen, Harrogate, and Leamington, the arsenical waters of Levico, the waters of Wiesbaden, and the muriated sulphur waters of Aix-la-Chapelle, deserve a trial.

The subject of the Wiesbaden waters will be referred to in a subsequent chapter.

### SODIUM CHLORIDE AND THE BIURATE— SIR W. ROBERTS' VIEWS.

Thanks to the diffusibility of common salt, which allows it to be separated from the blood and discharged through the kidneys with great rapidity, a fixed proportion of sodium chloride, which healthy blood tenaciously retains, is never much exceeded. Beyond this blood serum will not allow itself to be permanently charged. On the other hand, whilst any overdose would lead merely to a temporary surplus, any deficiency in the intake would have to be made up to the blood from the tissues. Sir W. Roberts

quotes on this point the results of Dastre and Loye,\* who have shown that, if not otherwise supplied, the blood will extract salt from the less vital fluids and tissues, and that, if over-supplied, it will discharge some of the excess into the serous cavities pending the restoration of the normal equilibrium by the kidneys. On this showing, he points out that a diminished intake of salt, whilst not materially altering the proportion present in the blood, would considerably lessen its proportion in the synovial fluids and in the fibrous tissues.

The Influence of Common Salt as an Article of Diet in Gout and Gravel.—Assuming, then, that in health it matters little whether we consume much or little salt over and above the bare requirement, the further question arises as to the influence of sodium chloride in gout. According to Sir W. Roberts' investigations, solutions of salt exert no influence whatever on crystals of free uric acid, but their influence on the solubility of the sodium biurate is most marked: in his maturation experiments so small a quantity as O'I per cent., or even less, added to blood serum, appreciably hastened the precipitation of the crystalline biurate. Consequently the amount of sodium chloride moving in the economy is not regarded by him as a matter of indifference in gout; at the approach of any threatenings of uratic precipitation, if it were possible, it would be desirable to keep down its percentage in the joints most threatened. Sir W. Roberts does not therefore hesitate to recommend gouty patients to restrict as far as possible the use of common salt at their meals.+ Since no harm attaches to

\* 'Lavage du Sang :' 'Archives de Physiologie,' 1888, p. 93.

<sup>†</sup> Between this recommendation and the danger of completely depriving the joints of their normal amount of sodium chloride, there is a wide margin. Yet, to secure any effectual diminution within them, the percentage of salt in the economy would have to be lowered, by

retrenchment, and as an excessive use of salt must be regarded with suspicion, great moderation is obviously the wisest course, in gout.

In gravel, an affection which is regarded by Sir W. Roberts as alternating rather than coinciding with gout,\* the influence of sodium chloride is totally different, and the indications for its use are exactly opposite. Although salt possesses no solvent power for solid uric acid, it retards the decomposition of quadriurates, and therefore the precipitation of uric acid. This explains the remarkable immunity of the inhabitants of the 'marshland' of Norfolk,† where the water is brackish, and that of seafaring men, who take a prodigious amount of salt with their food, and the no less remarkable frequency of stone among the natives of India, who live on rice, of all food-stuffs the poorest in mineral constituents (only 0.39 per cent.),‡ and among the poor in general.

Precipitation of uric acid is also favoured by a deficiency in the urinary pigments, by a high percentage of uric acid, and, above all, by the degree of acidity.

The influence of a minute addition of an alkaline bicarbonate in *postponing* the precipitation of uric acid is shown in Sir W. Roberts' tabulated observations:

very strict rules of diet, to an extent not free from all risk. Moreover, further evidence is needed as to the relative facility with which synovia and the joint structures would allow themselves to be deprived of their sodium chloride.

<sup>\*</sup> Mr. C. Plowright, 'On the Cause and Distribution of Calculous Disease,' London, 1886 (quoted by Sir W. Roberts), points out that Norfolk, one of the chief 'stone' districts, has a comparatively small gouty record. In Scotland, where gout is rare, stone is common.

<sup>†</sup> Cf. Plowright, Medical Times and Gazette, October 10, 1885.

<sup>‡</sup> The relative quantity of mineral matter is, for meat and fish, 5 to 5'50 per cent.; for milk, 5'50; for oatmeal and for potato, 2'50; for wheaten flour, 0'51 only (Roberts).

		Time of beginning precipitation (hours).		Postpone- ment (hours).	
No. 1 urine (no addition)	-	-	2	_	
No. 2 urine (added: 0.04	per	cent.			
potassium bicarbonate)	-	-	4	2	
No. 3 urine (added: 0'04	per	cent.			
sodium bicarbonate)	-	-	5	3	
No. 4 urine (added: 0'04	per	cent.			
lithium bicarbonate)	-	-	10	8	

In all these urines litmus-paper hardly showed any change, so small was the proportion of the alkaline addition. The difference in the delays recorded is described as a mere question of atomic weight, and of saturating power of the several salts.

The Influence of the Muriated Mineral Waters in Gout and in Gravel.—On the basis of the chemical observations which have been detailed, cases of gravel and of stone would derive the greatest advantage from the internal use of the muriated waters, and especially of those containing alkaline bicarbonates in addition; but in gout the circulation of so much additional sodium chloride might lead to a recrudescence of the symptoms by favouring the precipitation of the biurate.

#### GENERAL CONCLUSIONS.

In practice the theoretical objections which have been urged have not been confirmed by experience in a degree sufficient to deter all gouty patients from the use of the waters. The reasons for this discrepancy between the results and the theory are not far to seek. The hydration of the tissues and the flushing of the lymphatics, including those of the gouty joints, by copious and systematic supplies of water, introduce an element which is antagonistic to the tendency to sedimentation, and the latter is also

counteracted in many by the active life which is an essential part of the cure.

Moreover, many of the muriated waters are also feebly carbonated, and convey the antidote together with the poison, if the latter expression could be applied to common salt.

There is, however, another and more important aspect of the cure. Gout, as we have often insisted, does not begin at the uric acid stage; there is an antecedent factor. Water, as Garrod has himself pointed out, 'stimulates the entire metabolism, increasing the various secretions. To this general action the mineral constituents add their own special influences,' which in the case of sodium chloride is admittedly a stimulating influence. Any danger to be dreaded from the precipitation of the biurate may thus be happily forestalled by obviating, through an improvement in the metabolism, the excessive production or accumulation of uric acid itself. By checking the mischief at the fountain-head, we are spared the task of correcting its later developments.

#### CHAPTER LV.

# THE USES AND SELECTION OF MEDICINAL SPRINGS (Continued).

#### THE SODIC CARBONATED WATERS.

Sodium is the metal to which the alkaline waters owe their alkalinity; any question as to its action in gout opens up the question as to the suitability of the whole group.

Objections have been urged against it, which may be classed as clinical and chemical. The stronger sodic waters have been accused of occasioning a recrudescence of the arthritic trouble, of imperfectly relieving visceral gout, and of producing more than the usual nervous disturbance, or even definite nervous complications. Some of this criticism may have been over-anxious, and in some instances not free from partisanship. It should be remembered, as suggested by Lyman, that any spring of world-wide fame, such as Vichy, must attract not only the greatest numbers, but among them also the worst cases; and it is notorious that the latter are not always the best suited for energetic treatment.

Among the clinical objections, it is alleged that the strong sodic waters are exciting and congesting; that if given in sufficient dose to influence the dyscrasia they are debilitating. Lastly, it is thought of some of them that they are apt to constipate. The subject of the alleged alkaline cachexia

has been already discussed. The other objections deserve to be carefully weighed. It must be admitted that even the physicians who prescribe the Vichy waters do not contend that they are suitable to all stages, as this is claimed elsewhere for some other waters. The supposed constipating effect is one which it might be possible to remedy; nevertheless, it may sometimes account for an imperfect relief of the general and local symptoms in gout.

It has not been disputed that the stronger alkaline waters are the most potent in the treatment of gravel and of urinary concretions, although they no longer enjoy their previous monopoly in this respect.

The most, then, that can be said against these waters—against the Vichy and Vals waters in particular—is that they are not always well borne by debilitated subjects; that they are not suited to acute stages; that they may sometimes prove insufficiently laxative, or even constipating. In some cases, probably those of idiosyncrasy, they may not be easily digested, and may set up various nervous symptoms.

The chemical objection is a formidable one. It has been fully stated by Sir W. Roberts, and we have referred to it in previous remarks. An excess of sodium in the system, per se, might doubtless favour the formation and precipitation of sodium biurate, but we may repeat that 'everything depends upon the circulation.' If the sodium bicarbonate, and if the uric acid itself, can be kept moving, the danger in question is to a great extent averted. Any sudden check to the lymphatic circulation might conceivably, in a person over-saturated with sodium, lead to an easier precipitation of the biurate. So long, however, as the excretory organs are in full activity, and the liver relieved by a sufficiently laxative treatment, the general advantages of sodium may be secured without any serious

arthritic danger. Much will depend upon the degree of dilution, and upon the nature of the other mineral constituents of the waters.

The empirical reputation enjoyed by sodium has received a striking illustration in connection with a celebrated mineral spring which happens to lack the sodium bicarbonate. The attempt has been made to improve upon nature in this respect. Hitherto we had been content with raising the temperature of mineral springs for bathing purposes. The new departure of adding a fresh chemical constituent is a shock to sentiment in connection with mineral waters; but it conveys a practical lesson. The flattery of imitation reflects the opinion entertained at Wiesbaden of the value of Vichy waters in connection with their sodium salts. The 'Wiesbaden gout-water' is doubtless an excellent, though an artificial, combination; but it has out-Vichied Vichy by raising the proportion of the sodium bicarbonate from 5 (Célestins) to 8 pro mille.

#### MORDHORST'S VIEWS AS TO THE VALUE OF SODIUM BICARBONATE IN GOUT.

Mordhorst,\* who is a strong advocate of the artificial Wiesbaden 'Gicht-wasser,' uses the following arguments, among others, in favour of the administration of sodium bicarbonate:

- 'I. Increased alkalescence of the plasma, and consequently also of the tissue cell contents, augments their capacity for absorbing and retaining oxygen, thereby assisting and increasing the processes of oxidation and
- \* 'The Remedies which are applicable in the Treatment of Gout and Uric Acid Concretions, and their Mode of Action:' a lecture delivered at the Eleventh International Medical Congress in Rome, 1894; with a postscript by Carl Mordhorst, M.D. Kiel, Wiesbaden; translated by Ronald E. S. Krohn, M.D. Lond. Rome: Loescher and Co.; 1895.

decomposition. It is evident therefore that, with a diminution of the quantity of uric acid in the fluids of the body, the danger of its precipitation and deposition in the tissues is, other conditions being equal, proportionately diminished.

- '2. The fact, demonstrated by Maly, Chabrié, Runeberg, Hoffmann, and others, that acids and acid salts diffuse and filter more rapidly through animal tissues than do bases and alkaline salts, explains the circumstance that in gout, where the alkalinity of the blood is abnormally low, those tissues which are not supplied with blood capillaries, and only communicate with them by osmosis, namely, the fibrous tissues, must be less alkaline, often neutral, or even acid in reaction, and must be predisposed to the deposition of urates.
- '3. The more alkaline the tissue plasma is, the greater is its power to keep uric acid in solution.\*
- '4. The more alkaline the tissue plasma of the body is, the greater is the decomposition of any already formed uric acid. The correctness of this statement has been proved by the experiments of a large number of authors. They all found a considerable reduction (up to 30 per cent. or more) in uric acid after the administration of large doses of bicarbonate of soda.
- \* 'The startling results obtained by Biesenthal in his experiments on cocks and pigeons, which had been simultaneously treated with piperazine and neutral potassium chromate, show that it is possible to prevent the deposition of uric acid which results from subcutaneous injections of potassium chromate, according to Ebstein's procedure, by the administration of large doses of piperazine, and even to dissolve any such deposits when already present. The heroic doses given to the animals experimented on, viz., 0.5 gramme to the cocks, 0.2 to 0.5 gramme daily to the pigeons, calculated in proportion to the body weight, would correspond to 30 to 75 grammes for an adult weighing 75 kilogrammes. There can be no doubt but that, after such treatment, the tissues of the animals must become markedly alkaline' (Mordhorst, loc. cit.).

- '5. Biurates\* (in needle crystals) are, as well as uric acid, far more soluble in o.6 to o.8 per cent. solutions of sodium bicarbonate than in either stronger or weaker solutions or in distilled water. In the latter they are decomposed, uric acid being precipitated and the solution becoming alkaline.
- '6. Large doses of potassium carbonate cannot be given, as they depress the heart's action. Lithium, according to Paul Binet, t is the most poisonous of all alkalies and alkaline earths. W. Stirling to considers lithium to be far more poisonous than is usually supposed to be the case. Posner and Goldenberg's § experiments prove that lithium carbonate reappears in the urine to a great extent as lithium chloride. Haig | states that in the living organism lithium exerts no solvent action on uric acid whatever. According to Rose, Ilthium forms an almost insoluble triple phosphate with bisodium phosphate or with the triple phosphate of ammonium and sodium. This much, however, is certain: on account of its poisonous properties lithium can only be administered in such small doses, that to speak of alkalization of the blood or lymph taking place after its use is out of the question.
- '7. There only remain, therefore, the carbonates of sodium. When taken in mineral waters, and when too much is not taken at a time, sodium bicarbonate is well borne. The water must, however, contain neither too

<sup>\*</sup> Roberts' quadriurates are regarded by Mordhorst as biurates in a globular form. Roberts' experiments with blood serum are, in his opinion, not conclusive; for both blood and serum become acid as soon as they leave the living body, even after alkalies have been added (Hoppe-Seiler and Landois).

<sup>†</sup> Gaz. Médic. de Paris, 1892.

<sup>‡</sup> Journal of Anatomy and Physiology, 1892.

<sup>§</sup> Zeitschrift für klinische Medizin, Bd. 13, Heft 6, 1888, p. 581.

<sup>|| &#</sup>x27;Uric Acid,' p. 30. London, 1892.

<sup>¶ &#</sup>x27;Chemical Analysis,' p. 15.

much calcium carbonate, nor too little sodium chloride; for Kleine has pointed out that it is possible by using sodium carbonate to abstract gradually a considerable amount of chlorine from the body. A removal of acids, in the true sense of the term, is the consequence of the administration of alkalies.'

In conclusion, Mordhorst claims that the Wiesbaden 'gout-water' has stood the test of practical experience; that it can be taken continuously for years, which is not the case with Vichy, Vals, Fachingen, and other calcareous waters, for they are often badly borne, producing constipation, inappetency, restlessness, etc.; that it contains nearly twice as much bicarbonate and fourteen times as much chloride of sodium as contained in the Célestins Spring, with one-fifth of the amount of lime salts, and double the amount of solid constituents, and nearly three times as much bicarbonate and eleven times as much chloride of sodium as contained in Fachingen water, with one-seventh of the amount of lime salts, and three times as much solid constituents; that it is the only water which will render even the most acid urine alkaline without causing it to become turbid; and that when taken even in moderate quantities (two bottles daily), it will exert a very much greater solvent action on calculi, even of large size, than Vals water.

The case thus made out empirically in favour of the use of bicarbonate of sodium must be admitted as out-weighing the theoretical objections which have been raised against it. It may be argued that just as the beneficial effects of sodium in gout are largely due to its effect on the liver, the intercurrent gouty attacks often witnessed at sodic mineral springs may be induced less by the sodium itself than by other constituents of these waters, which may cause in some subjects a primary gastric and hepatic disturbance, with gouty arthritis as its result.

#### CHAPTER LVI.

#### CONCLUDING REMARKS.

#### THE HOME SPAS.

PRACTICAL indications for a selection of springs may be gathered from what has preceded.

In plethoric gout associated with imperfect action of the liver, or chronic hepatic congestion and its attendant symptoms, the order of efficiency of the springs would be as follows: the alkaline sulphated, the alkaline earthy, the muriated sulphated, and the sulphurous springs. The alkaline springs are also available, but additional medication may be needed besides the waters; and here, more even than at any of the other resorts, the constant advice of a competent physician is indispensable. The indifferent waters will also prove of advantage within the range of their capabilities, when supplemented with any necessary medicinal adjuncts.

Where acidity predominates, whether of the stomach or of the secretions, the alkaline waters are indicated. But they are not the only means of treatment. Here, again, the indifferent waters may effect much on the 'washing-out' principle; but more direct good will accrue from the alkaline earthy springs. With all due precautions, the sulphurous springs may also prove beneficial.

Uratic concretions of all kinds are treated by the alkaline and by the alkaline earthy springs.

Diabetes and glycosuria are widely benefited by various springs, a great deal of the good being dependent upon the attention paid to diet. Any mild action taken on the liver is always beneficial. The most celebrated resorts in these affections are Neuenahr, Carlsbad, Wiesbaden, Vichy, Vittel, Contrexéville; and their treatment from the nervous side is also represented at the various arsenical springs.

The same indications which apply to foreign resorts will be our guides in the selection of the British springs. These deserve special notice owing to the greater numbers, and to the longer time for which some of them are available.

#### THE MEDICINAL SPRINGS IN GREAT BRITAIN.

The British spas can often be reached by those whose opportunities do not allow of distant travel. Many have not the means of attempting a long journey or of meeting the expenses incidental to a residence abroad. Again, those more advanced in years are unfit or disinclined for so great a change. For all these the home resorts present the facilities required—hospitals being provided for the needy, and house accommodation proportionate to every income.

The Air-Cure and the Water-Cure.—An excellent air-cure for convalescents may be made at Clifton, Malvern, Tunbridge Wells, Matlock, Buxton, and many other places.

The water-cure is that most universally indicated in all forms of gout. Putting aside Matlock, where the waters only reach 68° Fahr., Bath and Buxton are the chief representatives of the best form of water-cure, the thermal.

Bath has a reputation as ancient as the history of Great Britain, and which shows every sign of increasing. Its waters are the hottest in this country, ranging up to

120° Fahr. They are available the whole year round; but spring and autumn are regarded as special seasons for treatment.

The Buxton waters are supposed to have been used by the Romans, but had not been in fashion until the end of the sixteenth century. Buxton's bracing climate adds greatly to its value as a health resort, but restricts its benefits to the summer season. Although the constituents of the waters are varied, they are present in such small quantities as to be, with the exception of iron and calcium, probably inactive.

At both resorts the internal use of the water is combined with its external use, which may be regarded as the most valuable.

A large number of gouty patients, for whom more energetic treatment is not needed, will be benefited by the watercure; and the same applies to those suffering from the various troubles of goutiness, although neuralgic patients, as often happens, may-especially at Buxton-suffer at first a slight recrudescence of pain, probably connected with the exciting effects of the air and of the treatment.

Although in Great Britain the groups of mineral waters are not all represented, considerable efficacy attaches to those which we possess.

The most important are the thermal springs of Bath and Buxton, and the sulphur and sodium chloride springs of Harrogate and Strathpeffer (both these spas also have chalybeate springs), and of Llandrindod, which also has important saline and chalybeate waters. Llanwrtyd, Builth, Moffat (near Dumfries), and Lisdoonvarna (in Ireland) should not be forgotten among the sulphurous springs.

Cheltenham\* is the almost solitary representative of

<sup>\*</sup> Cf. Dr. Archibald E. Garrod's report in 'The Climates and Baths of Great Britain,' p. 589.

the sulphurated saline group; it has been strangely neglected, although at one time a flourishing and useful resort. Cheltenham also possesses a chalybeate spring at the Cambray Spa.

The Leamington waters are of the sulphated muriatic type, and compare with those of Homburg, Kissingen, Soden, Salins-Moûtiers, and Wiesbaden,\* but are richer in magnesium sulphate than most of these.

Lastly, Woodhall Spa claims special virtues in connection with the bromine and iodine which its waters contain, and with their temperature.

Various other spas—an account of which will be found in 'The Climates and Baths of Great Britain'—need only a brief mention. The most important of these is perhaps Droitwich, which is not, however, specially indicated in ordinary cases of gout. Nantwich also has brine baths, and the baths of Stafford and of Saltburn belong to the same group.

The springs of Ashby-de-la-Zouch and Tunbridge Wells are chalybeate; the former are also muriated. Wales is further represented by Llangammarch Wells, noted for its chloride of barium.

Medicinally, the home resorts fulfil some of the indications which have been sketched. Bath and Buxton will be the resorts safely and successfully visited by every variety of gout. Cheltenham would represent the alkaline sulphated springs, such as Carlsbad, and would meet the requirements in cases of hepatic inactivity, with all its complications. Leamington will suit similar cases, though with much milder effect.

Harrogate and Llandrindod head the list of the sulphurous springs; their capabilities in the treatment of gout are considerable, because combining the air-cure

<sup>\*</sup> Cf. Dr. Archibald Garrod, loc. cit., p. 585.

with the water-cure. Acute gout is, of course, not suitable, nor cases barely convalescent; but most forms of chronic articular gout, many chronic visceral complications, gouty nervous affections (particularly neuralgia), and, above all, gouty cutaneous affections, will variously benefit from the internal and from the external use of the waters. Similar advantages on a smaller scale are also obtainable at Strathpeffer and Moffat.

Both Harrogate and Llandrindod have the additional advantage of chalybeate springs suited to the later stages of convalescence of some cases of chronic gout.

Woodhall Spa will probably rise to a position of considerable usefulness, and is already doing good work in connection with the chronic articular results of gout. Its chemical constituents give it a unique place among balneological stations in this country, and even abroad.

With certain reservations, and under medical guidance, great benefit may be obtained for some arthritic cases from the local treatment at the brine baths of Droitwich.

#### BRITISH SPAS FOR ARTICULAR GOUT.

For a large majority of the sufferers from articular gout and its various results the thermal water-cure at Bath or Buxton is the best procurable in this country. Between the two stations the selection is partly a question of seasons, Buxton being a summer resort, and Bath more largely visited in spring and autumn. It is also a question of the relative climates: the bracing air of Buxton would suit many patients better than the less stimulating air of Bath. In their internal as well as in their external uses the waters at both places may be regarded as fulfilling analogous indications, and their harmlessness is such as to render them available in cases where the more active springs are to be avoided.

Of very wide applicability are also the sulphurous springs, and particularly those of Harrogate and of Llandrindod, which are fitted with every facility for the thermal treatment. Owing to their constituents, they are not so universally tolerated. Still, whilst their contraindications are more numerous, their range of usefulness is extended to many other gouty conditions besides the articular.

The stiffness and thickening resulting from repeated attacks of arthritis are the chief, if not the only, gouty conditions for which the brine springs of *Droitwich* are utilized. Whether entire immersion into the heated dilutions of the brine should be permitted, or whether the treatment should be limited to the local bath or to the application of brine compresses, is a question to be decided after careful consideration in each case.

The waters of Woodhall Spa are also applicable to the same class of cases, and with analogous reservations. Their special virtues are supposed to reside in the bromides and iodides, but it is essential not to overlook the full charge of sodium chloride which they contain, together with some calcium and magnesium chloride.

Articular gout, especially in those of feeble powers but requiring some measure of treatment for the liver, and of help to elimination, will also derive benefit from a course at Cheltenham or at Leamington.

Cheltenham, which is probably destined to recover some of its former popularity, on the strength of the genuine value of its springs, enjoys a sheltered situation, which is a recommendation for many frail subjects.

Leamington has already secured by its modern improvements an important position as a balneological station. To various local attractions it adds that of its vicinity to many places of historical interest, and the charm of a picturesque country.

#### SPAS FOR GOUTINESS AND GOUTY AFFECTIONS.

The limited variety of our mineral waters is much more felt in the treatment of goutiness, with its multiple manifestations, than in that of articular gout. The specialization, to which we are accustomed on the Continent, of individual springs to the treatment of separate affections is a refinement unknown and unattainable. Most of all do we miss the alkaline, the alkaline sulphated, and the earthy sulphated springs. From this point of view a revival of the Cheltenham baths is much to be desired. Our insular isolation might almost be an excuse for following the example of Wiesbaden, and providing an artificial Vichy spring.

For the present, the gouty acid dyspepsia, commonly ordered to Vichy or to Vals; the chronic gouty gastric catarrh, for which Kissingen or Homburg are recommended; the plethora and hepatic congestion, for which Carlsbad or Marienbad are pre-eminent; the gravel and lithiasis, which Vittel and Contrexéville profess to cure as readily as Vichy, have all to be sent alike to Bath, Leamington, or Llandrindod, where special medication must supply the needful differentiation in the treatment.

The sulphur springs, which we need not again enumerate, fill with complete efficiency the place of the Continental representatives of the group in the treatment of gouty hepatic congestion, intestinal torpor, gouty catarrhs of the larynx, pharynx, and bronchi, gouty cutaneous affections, and some forms of gouty neuralgia and myalgia.

Gouty lumbago and other myalgiæ, gouty sciatica and neuralgiæ in general are successfully treated at Buxton and at Bath, at Droitwich, Woodhall Spa, and at other stations where the thermal treatment can be efficiently carried out.

For the important group of gouty diabetes and glycosuria, none of our resorts have yet equalled the reputation of Neuenahr, Vichy, Contrexéville and Vittel, and Carlsbad. The sulphur springs are not unanimously recommended. At Bath it is considered that the water is more suitable when deprived of its iron by cooling. Buxton has not established any strong claim in this direction. Much more success is reported from Leamington, and a trial of this spa can be safely recommended. The most efficacious of our mineral waters is said to be the saline spring of Llandrindod Wells. It is stated\* that not only do 'many patients suffering from diabetes frequent this spa every year on account of the improvement in their symptoms,' but that 'in some instances glycosuria is permanently got rid of by one course of treatment.'

Doubtless the properties inherent to some of our best mineral waters have not yet been fully worked out. For instance, we are still in doubt as to the value to be attributed to the *nitrogen* so largely disengaged by the Buxton waters, and to the chloride of barium which is distinctive of those of Llangammarch.

<sup>\*</sup> Cf. Dr. Frederick T. Roberts' report on Llandrindod Wells in <sup>4</sup> The Climates and Baths of Great Britain, p. 607.

### DIET AND HYGIENE IN THE PROPHY-LAXIS AND TREATMENT OF GOUT.

#### CHAPTER LVII.

#### DIET AND GOUT.

THE INFLUENCE OF DIET ON THE PREVALENCE OF GOUT AND OF GOUTINESS.

As stated in Chapter IV., two things strike us very forcibly in contrasting the contemporary history of gout with that of the last century. One is the increase in the numbers affected; the other is the mitigation of the forms noticed.

### THE INCREASED FREQUENCY OF GOUTY AFFECTIONS.

Gout is essentially a disease of civilization. This is a fact written large in the history of most nations. We have heard little of its prevalence among Spartans—and in the days of the Republic, Rome seems to have been exempt, whilst during the Empire the luxurious habits of living made it a growing scourge, even women, whose natural tendency to it is less than that of men, becoming largely affected. In modern times we have the testimony of explorers that it is unknown among savage races, and only observed in isolated individuals transplanted into the midst of civilization.

The second half of this century has been marked by an unprecedented extension of the luxuries of life; the law which has been stated would suggest a corresponding increase in the numbers affected; and such is the result we observe. There may have been error of judgment on the part of those who see something of gout in almost every patient. In itself, over-anxiety not to miss the diagnosis is a tolerably sure indication that the real disease has been too often met with and sometimes overlooked. Have we not witnessed the same tendency during the great prevalence of influenza? Influenza was wrongly diagnosed as present very much in proportion to the prevailing frequency of the affection. Even the most critical observers will probably agree in recognising not only an increased prevalence of gout and goutiness among the upper classes, but its wider extension to strata previously less affected.

Gout among the Masses - The Poor Man's Gout. - In speaking of the influence of social status, Sir A. Garrod inclines to regard the poor man's gout as one connected especially with impeded excretion, whilst the rich man's gout would be due mainly to increased supply and accumulation of uric acid. This distinction will probably remain true always, so long as the really poor are with us; but in this country at least it is tending to become less absolute. It is well known that the dietary of the lower classes has undergone considerable improvement. enormous importation of meat at a relatively low price has led to a considerable increase per head in its consumption. The well-to-do take probably not much more than they used to consume, and paupers or the very poor are probably still largely debarred from a meat diet. The increased consumption thus falls to a section of the lower class whom circumstances favour, and their share in the

increase is probably in excess of that which appears in the returns calculated per head of total population.

What is true of meat is equally true of most other foods, but specially of saccharine and fatty foods, in addition to eggs.

#### THE ATTENUATIONS OF GOUT.

On the increased prevalence of gouty affections among the upper classes it is unnecessary to dwell. The most remarkable features are: (I) The lessened frequency of the more severe manifestations; (2) the milder type of the acute attack; and (3) the greater predominance of conditions which may be described as 'attenuations of gout,' or 'goutiness,' in which there may have been just enough of the articular trouble to identify their gouty origin and character, but which for the rest run an abarticular course implicating various organs and functions, and specially the nervous system.

For these changes various explanations may be suggested. It is an undoubted fact that health has been more of a study. Even the gouty, whose memory for their past suffering is particularly short, have shown less recklessness, and been guided in some degree by the enlightened advice of physicians. They have, as a class, attended more to diet and to hygiene. The total abstention from wine in favour of whisky, which has been largely practised, has probably aided the result. A diminution has occurred in the severity of the seizures. The benefit gained has in some measure been enjoyed by the offspring, and inherited gout has probably become less severe.

To these influences should be added that of the modern forms of medicinal treatment. Chemical antidotes have not only helped to reduce the severity and the duration of the acute attack, but cautiously administered during periods of freedom, or at the earliest indications of a return, have procured many a respite from fits which otherwise had been unavoidable. In this happy result the systematic use of appropriate mineral waters, and periodical visits to the medicinal springs, have doubtless had a share.

Meanwhile, however, the great stress thrown upon the nervous system by the peculiarities of modern life seems to have brought about increased susceptibility to the influence of the irritating material, and in a fresh direction. The great toe has ceased to be in many cases the seat of least resistance, weaker spots having developed. In other words, a dose of poison hardly sufficient to determine a true podagra has been enough to call forth elsewhere less sharply-defined manifestations. In this way, whilst the causes leading to gout have multiplied, and the number of those affected increased, the major attacks of the disease have diminished in frequency, and the minor gouty ailments are more and more coming to the front.

### THE INFLUENCE OF DIET IN THE PRODUCTION OF GOUT.

A competent knowledge of the influence of diet on the production of gout would help us to guard against the affection. Our endeavours for its relief would also be better guided, although the methods of prophylaxis and those of treatment are not identical. Gout is commonly acquired with the help of a sound stomach, but, for its cure, a healthy digestion is no longer at command, and in daily practice dieting the gouty patient is as difficult as it is important. It will be well, then, to deal with the ætiological and with the therapeutical aspects of dietetics in succession, beginning with the former.

The derivation of gout from habitual excess in alimentation was well known to the ancients, and we still hold to the same broad, common-sense view of the subject. But the attempt to define the principles of diet on the lines of the uric acid theory has led to a conflict of opinions which suggests that we lack either sufficient knowledge, or sufficient regard for that which is definitely known. In gout, more than elsewhere, because of its idiosyncrasies, we should beware of dogmatism. Gout is undoubtedly prevented by starvation; yet it does not follow that it may be cured on that plan. Gout may also be prevented by strict avoidance of animal food. This does not prove that it need in every case be treated on vegetarian principles. Again, although gout may fail to attack some of those whose diet is exclusively animal, we are not warranted in prescribing meat as the diet for gout.

Each case should be studied on its own merits; but it is essential that we should grasp the main principles which underlie all individual variations.

'Great eaters are liable to gout, and of these the costive more especially. Eating as they used to eat when in full exercise, their digestion is naturally impaired. Even in these cases simple gluttony and the free use of food, although common incentives, by no means so frequently pave the way for gout as reckless and inordinate drinking.' In these lines of Sydenham is compressed the greater part of our practical knowledge. Neither the quality of food nor its quantity do so much harm as the fact that it is unearned by muscular exertion. Mental work is hungry work; but it does not fulfil the letter of the law that we shall earn our bread by the sweat of our brow. The idea that close study is productive of gout is probably erroneous. Intellectual labour is not harmful in itself, but only in the measure in which it excludes the needful muscular work, and the tonic influence of an outdoor life.

The second factor noted by Sydenham is constipation,

by which we may understand inactivity of the liver as well as of the intestine.

A third and prominent influence is that of the *impaired* digestion, to which we may trace the acidity of the gouty state.

The fourth factor is the abuse of *alcohol*, most active for harm when combined with excess in alimentation, and co-operating with the latter in checking the energy of metabolism.

All these are acquired facts, but their mode of operation is a mystery. By what mechanism is gout produced? The end product being an excess of insoluble urate, research has been steadily devoted to tracing the pathological history of uric acid, with results to which we shall presently allude.

The broad conclusions to be drawn from Sydenham's observations are that the failure of the digesting and assimilating functions arises from their *inadequacy* to deal with the relative surfeit of food; and that the food which is strength to the healthy man becomes *poison* to the gouty. Two questions are now before us: (I) What is the poison? (2) Which is the food which supplies it?

If, as alleged, the offending substance is uric acid, either introduced as such, or subsequently derived from food, meat would be its most plentiful source. We are not sure, however, that uric acid is not merely a by-product in gout, and that the more active agents are not those which escape our notice owing to their greater solubility. The ptomaines and leucomaines are types of the substances to which we allude, and their chief source is again animal food.

#### CHAPTER LVIII.

# THE VARIOUS CONSTITUENTS OF FOOD IN THEIR RELATION TO NUTRITION AND TO GOUT.

In addition to the water and to the mineral and organic salts which they contain, our foods consist of nitrogenous and of non-nitrogenous principles; and the latter are of two kinds—hydro-carbons (fats) and carbo-hydrates (starches and sugars).

The Non-nitrogenous Principles.—It is chemically impossible that these bodies should, independently of others, give rise to any uric acid when introduced into the economy as food; and this fact has been amply illustrated by experiment. Since, however, they cannot sustain life without additional supplies of nitrogenous substances, their suitability as articles of diet in gout is not a self-evident proposition.

The Nitrogenous Principles.—These are the generators of urea, and indirectly of uric acid also. It is now amply proved that their consumption on a large scale is followed by an increased production of uric acid, and that the latter diminishes when the supply is restricted. There is also no doubt that the increase in uric acid occurs in connection with the consumption of vegetable albumens, as well as with that of animal albumens, although the resulting amount of uric acid need not be, weight for weight, the same in both cases.

Many of our food-stuffs contain all three principles; others, two out of the three. The following table shows the proportion of the nitrogenous constituents of some of the more usual articles of diet:

### AVERAGE PERCENTAGE OF ALBUMINOID MATTERS IN VARIOUS FOOD-STUFFS

(COMPILED BY SIR W. ROBERTS FROM PAVY AND KÖNIG).

			Animal.			
						Per cent.
Butcher's	meat	-	-	-	-	- 19
Fowl	-	-	-	-	-	- 20
Game	-	-	-	-	-	- 22
Fish	-	-	-	-	-	- 17
Eggs	-	-	-	-	-	- 13
Milk		-	-	-	-	- 4
Cheese	-	-	-	-	-	- 30
		1	Vegetable.			
						Per cent.
Bread	-	-	2	-	-	8
Oatmeal	-	-	-	-	-	12
Rice	-	-	- 1	-	-	6
Green pe	as -	-		4	-	6
Potatoes	-	- 2	-	-	-	2
Carrots a	nd turr	ips	-	-	-	I to 2
Green ve	getable	s and	salad	-	-	I to 2
Fresh fru	it (excl	uding	nuts)	-		0'5 to I

When restricted to starchy food-stuffs, such as potatoes, greens, rice, bread, etc., we can still obtain a sufficiency of nitrogen, but the large bulk of food from which it has to be extracted will tax our powers of digestion. If, conversely, we were dependent wholly upon meat, the non-nitrogenous elements could only be found by using a comparatively large weight of it. This arrangement is generally regarded as unsuitable for gout, whilst that first mentioned, though not desirable, might perhaps stimulate

into activity the languid powers of digestion and of assimilation, and lessen the torpor which arises from never-failing supplies of the easier combinations of food.

# THE BEHAVIOUR OF THE VARIOUS FOOD-STUFFS IN GOUT AND GOUTINESS.

The Carbo-hydrates.—For the ordinary gouty subject, free from glycosuria and from obesity, starchy food in moderation is not in itself harmful. The glucose to which it gives rise is relatively well borne. The same cannot be said of cane-sugar, much more prone to ferment, and to liberate lactic acid. The gouty dyspeptic is often absolutely intolerant of starch and of saccharose, even when taken apart from other food. Others, whose digestion is but slightly impaired, will be able to use them with discretion.

Injudicious admixture with various indigestibles is really answerable for much of the fermentation of starches, and particularly for that of sugar. Acid wines, acid fruit, and elaborate sweet dishes, are specially obnoxious in this respect. Preserved fruit and jams, being heavily loaded with cane-sugar, are most apt to ferment.

Fats are to be used sparingly in gout. Here, again, great differences occur between individual subjects. Putting aside the dyspeptics who are quite intolerant, some will take fat in moderation with impunity, others are easily upset. Of all forms of fat, browned fat is the most difficult to digest (Duckworth), and for this reason fried fish and bacon are best avoided. According to Ebstein, there is no evidence that a moderate use of fat favours the production of gout.\* Great importance

<sup>\*</sup> The supposed detrimental action of fat in gout is discussed by Ebstein, who refers to the experiments of Meissner and R. Koch on the appearance of succinic acid in the urine after ingestion of calcium

attaches to its use as a guarantee that the organism shall not suffer in its capacity for exertion and resistance.

Ebstein permits meat and a corresponding amount of fat in the treatment of obesity and of gout, but limits the carbo-hydrates to a minimum. The carbo-hydrates save the albumen from complete destruction, part of it being stored as fat. Fats likewise save albumens, but in a far less degree than carbo-hydrates: 'That part of the albumen which is decomposed with the corresponding use of fat is decomposed completely, and does not remain in the body in an intermediate state as fat. Wherefore fat lessens the need for nourishment by protecting the systemic albumen, as Hippocrates was already aware.'\*

The increased need for food peculiar to a pure meat diet ceases, and the patient puts up with the curtailment of the excess of albuminates, and 'falls back on the right quantity of food,' so long as a suitable amount of fat is added to his diet. For this reason Ebstein allows fat together with the albuminates, whereas 80 to 100 grammes of bread should be the limit of the carbo-hydrate supply. Spinach, cauliflower, and red cabbage are the vegetables permitted in moderation; turnips, carrots, and beets are not allowed.

The nitrogenous foods are chiefly represented by meat and fish, and by cheese. The leguminous vegetables also

malate and of asparagin, together with large quantities of alkaline urates. The succinic acid appeared only after the ingestion of a surplus of fat; but the large quantities used were out of all proportion to the ordinary consumption of fat.

<sup>\* &#</sup>x27;The Nature and Treatment of Gout,' by W. Ebstein, M.D., Professor of Medicine and Director of the Medical Klinik in the University of Göttingen. Authorized translation by J. E. Burton, L.R.C.P. Lond., M.R.C.S., surgeon to the Hospital for Women, Liverpool; vice-president of the Liverpool Medical Institution. London: Baillière, Tindall and Cox, 1886. *Cf.* p. 164.

contain a rather large proportion of nitrogen. The questions relating to meat will be discussed separately.

Vegetables.—The slow digestion of vegetable fibre, the acidity of the vegetable juices, and the fermentation which they undergo, are responsible for much dyspepsia. Uncooked vegetables are inadmissible; and when vegetables are taken in conjunction with other food, they should be of the lighter kind only, free from fibre, and faultlessly prepared. Much might be done to render our vegetable alimentation more palatable, as well as easier of digestion.

In this country vegetables are regarded as mere adjuncts to meat; in France they are made to be a relish in themselves, fit to be enjoyed as a separate dish, when no meat is on the table. We might do worse than follow the example of a Devonshire father, who made a rule that vegetables should be served first, lest the children should eat too much meat.

Fruit is another source of acidity, the acid gastric fermentation coinciding with the alkalizing effect on the blood of the formation of carbonates from the vegetable acids themselves. Widely different notions have been expressed as to the effect of fruit on gouty subjects. Sir Andrew Clark was strongly of opinion that all fruit was harmful and promoted gouty symptoms. Others, on the contrary, see in its proper use a direct corrective. Much depends upon the variety and upon the quality of the fruit, and much also upon idiosyncrasy.

It is an elementary precaution to avoid in gout all indigestible fruit, and to use even stewed fruit sparingly. The late Dr. Milner Fothergill pointed out that stewed fruit might be used harmlessly if a proportion of bicarbonate of soda were added to each supply.

Among the varieties of fruit which may be allowed,

Sir A. Garrod mentions strawberries in small quantities, grapes, oranges, and other succulent fruits. He disapproves of all stone fruits, and of apples and pears unless baked.

We shall revert, in connection with alcohol, to the question of cider and of the virtues of apples.

Water and the Mineral Salts.—The value of frequent draughts of water, and especially of hot water, has been sufficiently dwelt upon in the therapeutical section. Hot water with meals agrees remarkably with some stomachs. The systematic water-drinking to which we refer is quite distinct from this practice, and should be reserved for fasting intervals, when there is no digestion to disturb. The objectionable hardness of many waters, which is regarded by some as prejudicial in gout, may be reduced by previous boiling, or simple aerated water may be substituted.

Chloride of sodium is the most important of the indispensable mineral salts. The majority of the latter are conveyed in sufficient amount in the food and in drinkingwater. Common salt itself is contained in food, and added to it in cooking. We have already dwelt upon the therapeutic aspects of the salt question. The consumption of salt is just one of those small matters which may tell by constant repetition. Sir W. Roberts, who recommends the lithuric patient to take as much salt as the palate will tolerate, would have the gouty use it most sparingly. There is great wisdom in this recommendation, the appetite hardly needing to be whetted in the average gouty patient; it is one, however, difficult to carry out, especially under the French system, so much depending upon the action of the cook.

#### CHAPTER LIX.

#### THE INFLUENCE OF DIET ON LEUCOCYTOSIS, AND ON THE RELATIVE EXCRETION OF NITROGEN, OF UREA, AND OF URIC ACID.

MUCH attention has been directed to the study of the effect of various kinds of diet upon the nitrogenous excreta, and in particular of uric acid, since Horbaczewski's discovery of the part played by the nuclein of leucocytes in the production of the latter. The following table embodies Horbaczewski's own experimental results:

TABULATED RESULTS OF HORBACZEWSKI'S OBSERVATIONS ON THE NUMBER OF LEUCOCYTES AND ON THE AMOUNT OF URIC ACID EXCRETED RESPECTIVELY AFTER EIGHTEEN HOURS' FASTING, AND FIVE HOURS AFTER A NITROGENOUS MEAL (A, A'), AND AFTER A NON-NITROGENOUS MEAL (B, B').\*

#### A .- Fasting.

Cases.	Leucocytes counted after 18 hours' fast.	C.C. urine (17th and 18th hour).	Uric acid (milli- grammes).	Total nitrogen (milli- grammes).
I	4,500	170	39'9	1,034
2	4,750	50	42.2	642
3	5,002	120	49.6	1,056
4	9,950	50	57'2	756
5	5,700	160	33'3	463

<sup>\*</sup> From Levison, loc. cit., pp. 15, 16.

A' (Same Cases).—After a Meal of Meat, Bread, Butter, Beer, etc.

Leucocytes counted 5 hours after meal.	C.C. urine (4th and 5th hour).	Uric acid (milligrammes).	Total nitro- gen (milli- grammes).
7,250 = +61'1%	340	148.1 = +271.0%	1,445
7,500 = +57'9	85	117.3 = +176.0	1,014
7,744 = +54'8	380	143.2 = +188.0	1,838
14,900 = +49'7	260	106.0 = +86.0	1,445
7,700 = +35'1	85	102.0 = +206.0	925

#### B.—Fasting.

Cases.	Leucocytes counted after 18 hours' fast.	C.C. urine (17th and 18th hour).	Uric acid (milli- grammes).	Total nitrogen (milli- grammes).
I	4,500	170	39'9	1,034
2	4,750	50	42.2	642
3	5,002	120	49.6	1,056
5	5,700	160	33'3	463

B' (Same Cases).—After a Meal of Vegetable Food only.

Leucocytes counted 5 hours after meal.	C.C. urine (4th and 5th hour).	Uric acid (milligrammes).	Total nitro- gen (milli- grammes).
5,900 = +23'1%	95	77.4 = +94.0%	869
4,900 = + 3'1	55	52.9 = +24.5	793
5,050 = + 0'95	280	59.3 = +19.5	1,159
5,850 = + 2'5	290	42.3 = +27.0	1,086

The tables A' and B' show a decided correspondence between the increase in the number of leucocytes and that in the amount of uric acid after a meal, whilst pointing to individual peculiarities in the proportion for each case. They further show that during the fourth and the fifth hour after a meal the increase under both heads is much less in the case of a non-nitrogenous than in that of a nitrogenous meal.

No conclusion could, however, be drawn from them as to the total excretion for twenty-four hours. We owe to Bleibtreu and Schultze\* a valuable contribution on this point. These observers determined their own total excretion of uric acid for twenty-four hours under vegetable and under animal diet. Bleibtreu's results were as follows:

	After 3 days' animal diet (grammes).	After 3 days' vegetable diet (grammes).
Total nitrogen excreted	24.4465	10'9217
Urea	47.3882	19.8082
Nitrogen in the urea	22.113	9.2432
Uric acid	0.859	0.791
Nitrogen in the uric acid	0.2863	0'2637
Proportion of urea to uric acid	1:55.16	1:25.04
Proportion of nitrogen of urea		
to nitrogen of uric acid	1:73.6	1:35.05

Schultze, whose habitual excretion of urea per diem was carefully estimated at 31.647 to 33.8549 grammes, and of uric acid at 0.836 to 0.844 gramme, reached, on successive days of an animal diet, the following amounts:

			Grammes.	Grammes,	Grammes.
Urea		 	58.89	67.23	73.65
Uric ac	id	 	1.3886	1'270	1.473

It is abundantly proved by these and other observations (Hirschfeld, Stadthagen, and others) that whereas the urea excretion rises with almost mathematical accuracy with the amount of proteids taken, the oscillations in the uric acid excreted are much more limited, and are not regulated by the diet. This is strictly confirmed by Dapper (cf. p. 100).

A valuable counter-proof was supplied by Busquet.+

<sup>\*</sup> Pfluger's 'Archiv.,' Bd. 45, p. 401 (Levison, loc. cit., p. 17).

<sup>+</sup> Revue de Médecine, 1892, p. 572 (Levison, loc. cit., p. 19).

The case was that of a chemist, who, by low diet, reduced his weight in the space of eighteen months from 107 to 74.5 kilogrammes, and his daily urea from 28 to 10 grammes. Meanwhile, the simultaneous determinations of uric acid made every day during the whole period yielded an almost constant figure (0.6 gramme), not falling below 0.4 gramme, and ultimately rising to 1.02.

After injection of 0.75 gramme nuclein, a rabbit passed 25.8 milligrammes of uric acid instead of the normal daily average of 7 to 8 milligrammes.

To test Maruss's observation that, after decreasing during the twelve hours which follow a meal, the uric acid excretion remains stationary for fourteen hours, a man was given 5.5 grammes nuclein suspended in water eighteen hours after a meal, when the excreted uric acid amounted at that time for two hours to 46.8 milligrammes:

During the first period of 2 hours after the nuclein was taken the amount was ... ... ... ... ... ... ... ... 46.9

During the second period of 2 hours the amount was ... 64.7

During the third period of 2 hours the amount was ... 93.6

The delay is explained by the slowly digesting nature of nuclein.

These experiments are almost conclusive in pointing to the leucocytosis which accompanies digestion as the source of the rise in the uric acid tide after meals.

This conclusion is supported by much collateral evidence, which may be summed up in the statement that an increased uric acid excretion goes hand-in-hand with an increase in the number of leucocytes—whether physiological, as in infancy and childhood (Martin und Ruge and Pfeiffer), and after ingestion of nuclein (Horbaczewski); or pathological, as in leucocythæmia (Laache, Bartels, Bohland und Schurz, Stadthagen, and others); in pneu-

monia and cancer and extensive burns, and after pilocarpin (Horbaczewski), after alcohol (Chittenden, Camerer, Levison), and after unusual physical exertion (Levison).

The same rule is confirmed by the diminution brought about both in the number of leucocytes and in the amount of uric acid by quinine and atropine. The only exception relates to the effects of antipyrin and of antifebrin, which produce an increase in the leucocytes and a reduction in the uric acid, presumably because under their influence the leucocytes may enjoy an unusual vitality, instead of breaking up early, as after pilocarpin, which also leads to splenic enlargement and karyokinesis in the lymphatics of the spleen.

Conclusions.—We should be taking too limited a view were we to connect the production of uric acid with the destruction of leucocytes alone. Some arguments which have been brought forward support with almost equal force the conclusion that uric acid is derived from disintegrative and metabolic changes in the totality of the organism—changes which, as stated by Levison, are influenced by alimentation, but not in the proportion of the nitrogenous ingesta, whilst the production of urea is strictly proportionate to the latter. According to this view the individual uric acid production would be for each subject a personal factor, remaining fairly constant on the whole, but subject to minor variations with each oscillation of the metabolism.

#### CHAPTER LX.

# THE VEGETARIAN TREATMENT AND THE 'MEAT' TREATMENT OF GOUT.

The labours which have been devoted of late years to the theoretical study of gout have led to some strange conclusions in connection with the practical questions of diet. We are assured by one authority that vegetarianism is the cure for gout, by another that butcher's meat is the true and successful remedy. This contradiction would almost suggest that the nature of the diet was a matter of indifference. It reminds us most forcibly that all cases are not to be treated alike; it enables us also to criticise without invidiousness both conflicting principles of treatment.

Both methods lean partly upon theory. Vegetarianism may be regarded as the logical outcome in dietetics of the uric acid theory of gout. The meat treatment finds support in the experimental evidence that an increased consumption of meat leads to an increase of the output of urea rather than of uric acid. These recent experiments have been described in Chapters XIV. and LIX. Their results are essentially identical with those obtained long ago by Lehmann, who found that the excretion of uric acid and of urea varied in the following proportions:

Under a mixed diet - - - 1 to 29
Under an animal diet - - 1 to 38
Under a vegetable diet - - 1 to 22

The physiological law which is thus clearly made out can hardly be used as the basis of a treatment of gout, unless it be assumed that excess of uric acid is the essence of gout, and of this we do not yet possess sufficient evidence.

Whilst both methods are more or less directly in touch with the uric acid theory, there is an apparent contradiction between the views put forth by Dr. Haig and the law that a vegetable diet gives a higher excretion of uric acid relatively to urea. For this discrepancy Haig offers an explanation. He points out\* that the relatively diminished excretion of uric acid under animal diet is due to raised acidity, this being the early result; but that in course of time the uric acid, meanwhile stored up, would be excreted again, and would then be greatly in excess; and that the relatively increased excretion under vegetable diet is due to the lowering of the acidity, which enables more uric acid to pass out. This increased excretion would gradually fall to the normal level after the stores of uric acid had been exhausted. As a fact, the production never varies much from the proportion I to 33 or I to 35.

Dr. Mortimer Granville does not regard the danger of increasing the acidity as an objection to the supply of butcher's meat. Assuming the normal urinary acidity to range from 2.5 to 3.0 pro mille, Granville finds in 500 gouty urines an average of 3.285: but 58 per cent. of the cases fall short of this average, and 41.5 per cent. exceed it, thus showing that the urine in gout may be less acid than that in health. These results were obtained in spite of an absolute avoidance of the alkaline treatment. The argument thus derived from the degree of acidity is perhaps open to the objection that the urine does not

<sup>\*</sup> Brit. Med. Journal, vol. ii., 1888, p. 10.

necessarily contain the full proportion of acid present in the system.

Haig's work\* gives a table of the quantities of uric acid which he has extracted from some of the animal tissues commonly used for food: Mutton (cold roast leg) contained '016 per cent.; veal (cutlet), '049; beef (cold sirloin), '016; beef-tea (treated raw), '019; meat-juice, '697; meat extract, '883.

Believing that the excess of uric acid in gout is derived from these and from analogous sources, Haig sums up the dietetic part of his treatment thus: 'The whole point of the diet treatment of uric acid disease is to cut out the butcher, and live by the baker, the dairyman, and the fruiterer; and if these things are well taken, urea will be kept at 3 grains per lb. of body weight (corresponding to a formation of about I grain of uric acid for 12 lb. of body weight), without the addition of eggs.'

The opposition between the arguments adduced is not less striking than that of the methods which they seek to support. We are induced to look farther afield for a rational explanation of the favourable results reported from both sides, and we find a plausible suggestion in Sydenham's view, that gout is dyspepsia: 'The more closely I have thought upon gout, the more I have referred it to indigestion.' Any relief to the dyspepsia would be some relief to the gout.

Both methods under discussion are remedies for dyspepsia—the one a radical, the other a palliative remedy. To simplify the diet to little besides meat would be to lessen the labour of the stomach, whilst ensuring proper support. To give up all meat, and learn to live and thrive on vegetable and milk food, would be to conquer at one stroke dyspepsia and the gout.

<sup>\*</sup> Cf. loc. cit., p. 355.

#### THE TREATMENT BY MEAT DIET.

Whilst recognising the advantages of a meat diet in cases of dyspepsia where starches, sugars, and fats are apt to set up acid fermentation, we cannot overlook the frequent instances of goutiness in which meat is distinctly obnoxious; neither can we put aside the accumulated clinical evidence which shows that a habitual excess of animal food favours the development of gout. A large consumption of meat may be kept up for long periods without giving rise to gout, especially if sufficient exercise be taken; and great moderation in animal food is not always rewarded by immunity. Again, absolute proof is wanting that it is the nitrogen in meat which produces the gout, though it undeniably increases the production of uric acid; and it is equally unproved that carbo-hydrates and fats do not take a share in the production of gout, although they are quite unable to supply any uric acid.

Nevertheless, when all this is granted, the broad clinical facts remain, that acquired gout is most common in those whose indulgence in animal food is excessive, and that it is, practically speaking, unknown among races who do not consume meat, and in persons who for a long time have been strict vegetarians.

In this country gout is usually acquired, with the help of a good digestion, and of just exercise enough to favour an appetite, on plentiful meat-supplies, coupled with an abundance of every other kind of food, and on wine or beer. This is the history of the well-to-do and of their butlers.

Among the lower class the amount of meat may not be so great or varied (though meat may find an equivalent as regards nitrogen in cheese). Almost invariably beer is the beverage; very often porter is drunk in addition to ale, or instead of it. Heavy muscular work is not a characteristic

of those of this class who develop gout. Their case is really not far different from that first described. They are relatively overfed, deriving their saccharine supplies with considerable regularity from beer, whilst they do not give up ordinary meat.

A feature common to both these diets is the abundant and regular supply of saccharine, which may often be almost equivalent to the body-waste, and yet is but a foundation for the heavy nitrogenous contingent of food and for the hydro-carbons, which are usually well borne and well digested. Thus the food-supply is partly of a very easily-assimilable sort (saccharine), partly of a high potential (nitrogenous).

In dealing with these various supplies the liver is fully taxed, often overtaxed; but it is doubtful whether, without the animal food, the hepatic difficulty would culminate in gout.

One of the strongest proofs of the gout-producing tendency of a meat diet is the prevalence of gout among the Parsees, who are large meat-eaters. Their liability to gout, in spite of the protecting influence of the climate of India, is rendered more striking by the immunity enjoyed by the natives, and even by those among the English who had suffered from gout in England, so long as they remain careful in their diet.

Until these facts can be explained away, we cannot admit that butcher's meat is the proper food for the gout, however helpful it may prove for a time for gouty dyspepsia with inability to digest other food.

#### VEGETARIANISM.

Of the value of vegetarianism for the cure of a variety of symptoms usually attributed to a disordered liver, but perhaps occasioned in susceptible subjects by the peptic products of animal food, there cannot be any doubt. In lithæmia itself a change to vegetarianism from the mode of living which brought about the unhealthy state, when carried out with earnestness and clinical tact, is a safe remedy, as successful as it is rational. The constantly recurring absorption of animal juices into a blood already overcharged with nitrogenous waste products keeps up the lithæmia. Vegetarianism strikes at the root of this evil by supplying the needful nitrogen without any of the waste products. The depression, the languor, the lassitude and unfitness for exertion, which are so many symptoms of nerve intoxication, quickly vanish, and the impaired powers of digestion are renewed.

The close relationship subsisting between lithæmia and gout, and the large share which we have attributed to the liver in the ætiology of the latter, would lead us to expect a similar benefit. To a limited extent this expectation has been realized. Patients have been known to remain free from gout so long as they adhered to vegetarianism and to abstinence from wine, and to relapse on returning to an animal diet. Few, however, seem to have made the experiment. It is significant that the greatest authorities on gout, from antiquity onwards, have been almost unanimous in their distrust of vegetarianism. Even Mead (1673-1754), who believed that in its earlier stages gout was curable by a milk and vegetable diet, generally allowed a small quantity of tender meat once a day. Gairdner thinks that a vegetarian diet, when attempted, has led to great aggravation of the patient's sufferings. Scudamore, Garrod, Lecorché, and Rendu have all expressed their disapproval of the method. Some of this discredit has probably arisen from the unsuitability of cases in which it had been tried. As pointed out by Sir Dyke Duckworth, patients of mature years are not fit

subjects for so great a change. Even the milk treatment is best tolerated by relatively young stomachs.

In addition to the idiosyncrasies of the individual which preclude any rigid uniformity in the dietary, we have to deal in gout with every stage and degree of the disease between the opposite extremes of gouty plethora and of gouty cachexia. In a large number of cases debility is the leading feature, and calls for the stimulation of animal food. Even in the remaining class, in which the complete avoidance of animal food might have the best results, vegetarianism is difficult to enforce, and irksome to practise, and a mixed diet, with a moderate supply of meat, will prove to be the only one suited for general application.

#### CHAPTER LXI.

#### THE PRINCIPLES OF DIET IN GOUT.

#### THE CHEMICAL PRINCIPLES OF DIET.

WE have sought to define the fundamental principles which must be regarded in constructing a rational dietary of gout. They are the following:

- 1. Nitrogenous food of all kinds, whilst it largely increases the output of urea, raises slightly the total output of uric acid, probably through increasing the total nitrogenous metabolism.
- 2. Animal food, taken in excess, favours the production of gout; taken in moderation, it is not usually harmful, but the reverse, to gouty subjects. The detrimental influence of animal food is not entirely, if ever, due to the uric acid which it contains, nor to the slightly increased production of uric acid to which it gives rise in about the same proportion as nitrogenous vegetarian food. More probably it is due to other factors, and perhaps to leucomaines.
- 3. Carbo-hydrates and fats, though incapable of transformation into uric acid, nevertheless influence the metabolism which gives rise to it. Gout being largely determined by disturbance of digestion, and consisting essentially in a faulty metabolism, they cannot be regarded as free from an active share in the production of gout, since they are largely responsible for the dyspepsia.
  - 4. A diet mainly of animal food, whilst simplifying in

many cases the work of gastric digestion, is productive of other consequences which render it unsuitable in gout.

5. A vegetarian diet, which generally supplies less nitrogen than an animal, or a mixed diet, does good chiefly by simplifying the process of digestion, by alkalizing the blood, and by lessening the accumulation and stopping the intake of the nitrogenous waste-products. These advantages are probably of greater value in gout than the mere reduction in the accumulation of uric acid.

#### THE GENERAL DIETETIC PRINCIPLES.

Man is omnivorous. His entire system of dietetics is based upon this fact. Whilst theoretically the purest blood is to be secured from the natural, non-animalized foods, free from all suspicion of contamination, we cannot disregard the existence of his carnivorous instinct and the practical advantages of an animal diet. Meat will therefore form part of his diet; but the amount to be taken will depend upon his pursuits, his surroundings, and, above all, upon the climate.

This omnivorous character, and the singular adaptability which he possesses, in a higher degree than any of the animals, for diet and for climate, also enable him to subsist on exclusive foods—at any rate for a time, provided they contain the indispensable proportions of the primary principles. In this way he can live on purely animal diet, or become a pure vegetarian. These are provisions of nature intended to meet special contingencies, not for common application.

The Proper Mixture of the Elementary Food-stuffs.—Milk is in this respect the type of all foods, containing abundant nitrogen in its casein, and abundant fat, sugar, and salts.

Persistent deprivation from any of the primary foodstuffs inevitably leads to weakness, or even to disease; scurvy is the most striking instance in point. This is not one of the causes or dangers of gout.

A mixture of the various classes of food is also an indication of nature, and this is a standing argument against vegetarianism. Whenever, owing to some accidental or constitutional cause, or to habit, a disability for certain classes of food exists, we should aim at restoring, if possible, that healthful variety in the supplies which is essential to the highest type of nutrition.

There is a moral side to digestion which must be thought of, as well as the chemical,—a gastric nervous system to cheer and stimulate, peptic functions to feed and to encourage, an assimilation to influence through the improved energy of the stomach. All these indications will be best fulfilled by our sanctioning the judicious use of aliments free from major objections, so long as they act as aids to digestion and raise the general tone, and with it also the general fitness for exercise. Thus, the severity of the strictest rules may often be relaxed with greatest benefit, so long as we can secure some corresponding advantage in the direction of muscular or mental hygiene.

A varied diet is the indication for the cure of diseases of nutrition, and eminently also for that of gout. In gout, however, where intolerance often exists for some special foods, due regard must be paid to the fact, though in respect of all remaining food-stuffs the utmost variety should be the aim to pursue.

Complexity of meals is not an indication of nature. Here, again, milk is the type of that simplicity which belongs to a natural dietary. The tolerance of a robust stomach for a large assortment of different foods at one meal is in itself a striking instance of the omnivorous power of man, but it is a facility which cannot be persistently abused without serious detriment. The practice

of loading the most nutritious viands with rich sauces and adjuncts is an evil from which escape is too often difficult in our modern conviviality.

The selection of food is, thanks to the unequalled opportunities of our civilization, carried to a high pitch. There is some danger in this perfection. Whilst luxuries should be the exception, many live exclusively on picked and dainty food, the chief fault of which is the ease with which it is absorbed. The powers of digestion are no longer exercised, as nature intends them to be, by the simpler and rougher food, the slow digestion of which affords neither scope nor desire for an undue frequency of meals. Again, with the coarser food, bulk is less apt to mean over-saturation with nutriment; the food is probably more fully utilized, and, so long as the stomach is equal to its digestion, is less apt to set up the artificial craving which is characteristic of overfeeding.

#### THE GENERAL DIETETIC PRINCIPLES IN GOUT.

In gout the same principles apply, with certain reservations affecting chiefly the mixture and the variety of food.

The quantity of food should be limited. Large eating does not always fatten people, neither does it always lead to gout. Why those (as for instance prosperous butchers) habitually using an excess of animal food, should sometimes develop obesity, and sometimes gout, is not explained by our theories, though we are now aware that fat may be derived from nitrogenous supplies. Where gout is established, moderation is essential. Large meals must be avoided.

For special kinds of food a relative disability is often developed in gout and in goutiness. Meat may no longer be tolerated as formerly, and some forms of it may, in given patients, set up marked disturbance. More generally

the saccharine constituents of food are a source of trouble, and have to be given up; while in all gouty patients acids, or any ingesta leading to acidity, are little short of poison; and even fresh fruit has been regarded as distinctly obnoxious.

Thus restricted, very little would remain for the unfortunate patient to live upon, and he would be sadly deprived of that variety to which we attach primary importance in dietetics.

Often, however, the disability is apparent rather than real. It is the mixture and the excess of food which the gouty stomach can no longer manage. Except in aggravated dyspepsia, any one class of food-stuffs taken separately will be successfully digested. This is the secret of the success of an exclusive meat diet, of an exclusive milk diet, and of pure vegetarianism.

Although none of these exclusive plans are permanently practicable, we learn from them that the essential principle of diet in gout is *plain food* and uncomplicated mixing of foods. For this reason the least easily-managed elements of diet—the carbo-hydrates and the fats—should not be taken promiscuously, and when combined with others only in small quantities and in the most simple form. This applies particularly to the sugars and to the fried fats, which will inevitably disagree if taken with much other food.

The Value of Change in Diet.—It is sometimes alleged that any interference with the habits of digestion and with the customary supplies may act detrimentally in gout by upsetting the function, and indirectly leading to gouty complications. In extreme old age it is, doubtless, wise not to interfere with the slender forces of digestion, which survive, as it were, on the strength of habit; and anything suggested should be strictly in harmony with the patient's instinct and experience. With gout at a less

advanced age, we need not be so timid. Laziness of the functions is the fault to correct. Any rousing influence, whilst it may temporarily discomfort, will ultimately benefit the patient. A similar result is witnessed at health resorts, where passing attacks of gout are followed by permanent improvement. If slight gouty manifestations should be brought about in consequence of variety in the diet, much will have been gained if the spell of habit has been broken: the stimulating effect of change is better than physic.

There is much that a patient can do for himself by occasionally varying the routine of his accustomed diet. In this connection it would be interesting to inquire into the therapeutic value of fasts, which were probably instituted in connection with some hygienic purpose. It is certainly remarkable that the time for the Lenten fast should coincide with that when the effects of an unduly nitrogenous diet are usually felt by those predisposed.

Again, as in diabetes, we must occasionally relax the restrictions of diet. A little cardiac and nerve stimulation, such as may be derived from the use of tea, coffee, alcohol, etc., which may have been withheld, and the cheering influence of variety, may, under ordinary circumstances, do much more good than harm. Nevertheless, there is a danger not to be lost sight of, lest habits which, if continued, are detrimental, should be resumed as a consequence of temporary indulgence.

#### CHAPTER LXII.

# THE DIETARY AND ALCOHOL IN GOUT AND GOUTINESS.

## THE SPECIAL INDICATIONS AND THE DIETARY IN GOUT.

The general principles which have been discussed are a safer guide in the management of individual cases than any detailed formulary. The variety of gouty ailments and of gouty states is such that the attempt to suggest sets of diets suitable to each requirement would be futile. The diet must be arranged for the individual case. Whilst the physician should cultivate freedom from rigid theory, the patient expects firm and definite instructions, and will be better able to follow them if they are written or printed.

Precise and complete rules, specifying the number, the time, and the composition of the meals, but above all what to avoid, are of lasting help to the chronic gouty patient; whilst in acute gout the diet has to be reconsidered each day. They are indispensable in the three important gouty diseases in which diet is the main part of treatment.

#### DIET IN ACID GOUTY DYSPEPSIA, GOUTY GLYCOSURIA, AND GOUTY ALBUMINURIA.

In all these cases certain limitations are unavoidable, but the least severe measures will often be the most successful. Our endeavour is to find out what our patient can safely manage, and how his strength can best be kept up, rather than to curtail too rigidly the supplies. In each case the best dietary can only be arrived at experimentally, and by special study. With this object, it is important that the food should be palatable.

Special restrictions are more easily carried out in bedridden cases than in patients who are going about. The daily expenditure of the latter is greater, and must be compensated; they must have sufficient food, and of a kind which they can digest.

Acid gouty dyspepsia in its worst form is one of the most troublesome of ailments. Its dietetic management does not differ from that of the non-gouty kind. Milk may be the only aliment well borne, and may even need to be peptonized. In other cases lean meat or fish is the chief article of diet. Vegetables, fats, and starches always disagree, unless taken in the smallest quantities and thoroughly prepared. Some of the infant foods may be tried with advantage.

Gouty albuminuria, in its milder degrees, does not call for any special diet, but merely suggests constant watchfulness in the avoidance of dyspepsia. Confirmed organic disease of the kidney is an additional indication for moderation in the use of animal food, but seldom implies a necessity for its suspension. In itself, the persistent drain of albumen rather points to a need for an adequate nitrogenous supply; but this should be of the least irritating kind. A judicious combination of the more digestible vegetables and fruits with the lighter varieties of meat and of fish, tends to lessen the acidity of the urine, and to increase the alkalinity of the blood. Any threatenings of uræmia are best treated by a short course of exclusive milk diet.

In gouty glycosuria and diabetes the strict diabetic diet is not appropriate. Neither its coarse and indigestible substitutes for wheaten bread, nor its heavy supplies of meat, are suitable for the delicate stomach of the gouty. If we can subdue the gout, the glycosuria will lessen, or even disappear. Thus, whilst the liver is treated medicinally, the digestion should be humoured. Well-toasted bread may be allowed, and sometimes even a moderate amount of starchy food. Sugar is best avoided; but the skilful use of saccharin will enable the patient to enjoy some of his favourite dishes without any harm. Here, again, a periodical resort to a milk diet is much to be recommended.

#### THE DIETARY OF CHRONIC GOUT AND GOUTINESS.

The average gouty person, whose condition is not that of a confirmed invalid under constant medical supervision, needs more than any other a clear notion of what is allowable and of what should be avoided. The following hints may be of service.

Meat and fish may be taken daily, in moderation, but it is much the safer rule to partake of them at separate meals—fish for breakfast or lunch, and meat for dinner. Neither salt meat nor salt fish is suitable. Salmon, eels, mackerel, and other heavy kinds of fish, are not desirable, and should only be indulged in occasionally. Boiled fish is to be preferred to fried; and the exquisite flavour of perfectly fresh fish will be best appreciated if sauces are wisely given up.

In the selection of meat, individual taste and digestive power are the chief guide. If the latter is fairly good, variety will be enjoyable and of use. Butcher's meat, which Dr. Mortimer Granville advocates to the exclusion of white meat, has the advantage of a greater nutritive value, and may be recommended to those who adhere to the rule of taking meat once daily, and in moderate quantity. The objection to fowl and game on the score of the slightly larger proportion of uric acid they contain should not be brought into line against the great advantage of variety, and against the special value which they possess for those whose feeble digestion is not always equal to the stronger animal food.

Vegetables, if properly digested, can only do good by their alkalizing and depurative effect on the blood. The avoidance of preserved and pickled vegetables, and of all coarse fibrous parts in fresh vegetables, is an elementary rule. Celery and lettuce have enjoyed a special reputation in gout. The majority of the common vegetables agree. Potato, peas and beans, artichoke, salsify, onion, turnip, greens, and particularly cabbage, are all allowable. Carrot and beetroot, which contain much sugar, must be used sparingly.

There is a group of vegetables which cannot be recommended to the generality of gouty patients, although individual tolerance may exist for some of them. Asparagus has long been regarded with suspicion. Opinions differ as to the nature of the irritant, whether simply oxalate of calcium, aspartic acid, or asparagin. This luxury is to be avoided, or used with great moderation. Tomatoes, rhubarb, and sorrel are exceedingly acid, and usually disagree; they contain an abundance of oxalate.

Fruit is theoretically indicated. Yet, apart from the idiosyncrasy which sometimes forbids the use of any, or of special kinds of fruit, in general all gouty subjects have to exercise much discretion in this matter. Fruit is inadmissible in the later hours of the day, and especially after a full meal, or in conjunction with wine. The safest time is the early morning before breakfast, or the middle

of a long interval between meals. Whether taken before or after meals, or as an intrusion upon the valuable periods when the stomach is at rest, fruit does not aid digestion; it is a complication, and we do not wonder at patients spontaneously or under advice giving up its use entirely. Exceptions are found to every rule, even with regard to fruit. Thus strawberries were considered by Linnæus\* to be antagonistic to gout, though generally found to be difficult of digestion. Apples and pears, disapproved, as well as all stone fruit, by most authorities, have enjoyed a reputation for the alleviation of gout, which is to some extent supported by practical experience. Grapes and oranges, which easily yield their juice without any of the indigestible substance being swallowed, are of all fruit the most suitable.

Baked apple and various kinds of stewed fruit may be taken, but not the sweet juice which accompanies the latter.

Of sweet dishes it need merely be said that they are unsuitable for the gouty in the measure of their elaborateness. To the simple puddings made with rice, sago, tapioca, and similar preparations, there can be no objection. Pastry should be avoided; its place might be taken by the harmless dry biscuits.

# THE EXCLUSIVE DIETS IN THE VISCERAL COMPLICATIONS OF CHRONIC GOUT AND GOUTINESS.

When some visceral complication, hepatic, renal, or intestinal, interrupts the even tenour of health, great advantage may accrue for the gout as well as for the visceral complication from a period of relative physiological rest for the digestion. This may be secured by combining with rest in bed abstinence from animal food,

<sup>\*</sup> Cf. Garrod, loc. cit., p. 396.

or, better still, an exclusive milk diet. In the former case, the full measure of the ordinary vegetarian diet might be allowed; in the latter milk only, with or without the addition of bread and light pudding. Although ill suited for gouty subjects able to lead a relatively active life, these simpler foods suit the lessened needs of the bedridden invalid, and relieve the overtaxed or weakened functions.

Sydenham does not allude to this temporary method, but gives us his experience of the continuous treatment by milk, of which he disapproves.\* None of the evil which he describes, but only good, can arise from the temporary restriction under the favouring influence of rest. A few days will suffice to effect great improvement in appropriate cases. Passive exercise and massage may sometimes be profitably combined with the milk cure, and the depurative action of the fluid diet may thus be greatly assisted.

#### THE USE OF ALCOHOL IN GOUT AND GOUTINESS.

It cannot be gainsaid that our prevailing attitude towards alcohol is a compromise. Alcohol is bad for the gout, but often good for the patient. Sydenham wrote: 'The old saw is that "If you drink wine you have the gout, and if you do not drink wine the gout will have you." The first part is true enough. It is proved by the experience of patients that wine is absolutely hurtful. . . . Add to

\* 'A milk diet (the milk being either raw or boiled), with nothing besides but a little bread, has prevailed for the last twenty years. It has done good so long as it has been rigidly attended to; the moment, however, that the patient swerves from it a hair's breadth, and the moment he betakes himself to the diet of a healthy man (no matter how mild and simple), the gout returns worse than ever. This is because the principles of Nature have been weakened, so that the disease becomes more obstinate and dangerous in proportion as the patient is unable to resist it.'

this the effect of wine (habitually taken) in making the body soft and loose like that of females; whereas temperate liquors so give tone and strength to the constitution that water-drinkers scarcely know what gout is.' But he adds, further on: 'This is a rule for the gouty: They may take those liquors which neither chill the stomach nor intoxicate in any moderate quantity. Such is the small beer in our own country, which in foreign countries may be replaced by weak wine-and-water. Water alone is bad and dangerous, as I know from personal experience. When taken, however, as the regular drink from youth upwards, it is beneficial. Those who take a diet-drink instead of beer may allow themselves greater latitude in the points of regimen.'

The principles laid down by Sydenham are almost identical with those which still guide our practice.

The Share of Alcohol in the Ætiology of Gout.—Alcoholism pure and simple in its extreme form does not generate gout. The spirit-drinking inebriate is exposed to more serious ills, among which gout is not included. This is perhaps to be explained by his habitually underfed condition, due to the weakening of the digestive function and of the appetite. This marked immunity is the more striking since, according to Hammond and Boecker,\* whilst urea is considerably diminished, uric acid either remains constant or is slightly increased by alcohol; and since leucocytosis, with which a rise in the output of uric acid is always associated, is among the results of the consumption of alcohol. The same conclusion has been pointed out in the chapter on lead intoxication.

According to Sir W. Roberts, alcoholic beverages in moderation exert no appreciable influence on the quantity of uric acid produced in the body; neither does the

<sup>\*</sup> Quoted by Rendu, loc. cit., p. 181.

admixture of any of them modify in any way the results of the experiments conducted with various fluids. He concludes (loc. cit., p. 125) that 'the special part played by some of them in the genesis of the gouty constitution, and in fostering a proclivity to uratic depositions, is evidently of a very subtle and complex character, and has apparently no direct reference to the chemical problems discussed.'

Whilst alcohol pure and simple does not produce gout, the fermented alcoholic beverages are known to do so. These facts point strongly to the important part played by the acid products of digestion as direct ætiological factors. Uric acid cannot be directly produced from alcohol, neither can it be produced from the constituents of wine; thus the different influence of the two beverages cannot be explained on the theory of uric acid excess. Again, were gout merely dependent upon a retardation of the metabolism, alcohol might have sufficed to have produced the affection; but we find that it does not. As pointed out by Sir A. Garrod, it is only the imperfectly fermented alcoholic beverage which promotes gout. The determining factor would thus appear to be the interference with healthy digestion by the acidity induced by wine or beer.

### PRACTICAL CONCLUSIONS AS TO THE USE OF ALCOHOLIC BEVERAGES.

In acute gout alcohol in any form is contra-indicated; the need for it may arise, but is exceptional.

In chronic gout the chief value of alcohol is dietetic. To a large number of patients, who have long been accustomed to stimulants, it is indispensable as a stomachic.

Whatever view may be taken of the alcoholic question in gout, the importance of securing a healthy digestion is paramount. Much, therefore, depends upon the right selection of the stimulant.

Comparative safety lies in avoiding all wines and malt liquors, and in trusting to that form of spirit which most closely approaches chemically pure alcohol. The best whisky, well matured, is therefore to be preferred; it is usually well borne, even when the liver is intolerant of brandy. A small quantity, diluted with water or with some light table water, may be taken at lunch and dinner. Nothing more is needed, and many gouty patients adhere faithfully to this rule with decided advantage. The monotony may be varied by substituting brandy or gin for whisky; individual taste will often be the best judge.

The selection of a suitable wine, where wine is indicated or desired in preference to spirits, is sometimes facilitated by the patient's own experience. Idiosyncrasy is apt to be as marked in respect to wine as in respect to articles of diet, and should be taken into account.

The qualities we should look for in a wine for habitual use are: a moderate percentage of alcohol\* and of ethers; the least possible degree of acidity; freedom from unfermented sugar as far as this is consistent with a natural unadulterated condition; freedom from tannin; genuineness as to vintage, or, at least, as to derivation, mixed wines being most likely to do harm; and, lastly, mature age.† The difficulty in securing these essentials is perhaps greater now than at any previous period, and adds to the strength of the general objection to wines in gout.

† Dr. Burney Yeo lays stress upon the fact which he has observed, that those wines agree best which act upon the patient as diuretics.

<sup>\*</sup> According to Duckworth (*loc. cit.*, p. 426), the average percentage of alcohol in spirits varies from 35 to 44; port wine has 19 per cent., madeira 18 per cent., sherry 17 per cent., champagne 11 per cent., burgundy 10 per cent., bordeaux and Rhine wine 8 per cent., porter 6 per cent., ale 3 to 6 per cent., and cider 4 per cent.

The gouty wines, which most depart from this standard, and which are found to disagree, are above all the sweet and heady wines of the South, which are not much used in this country; and among those in common use, port, sherry, madeira, and burgundy. Sydenham, who allowed a little wine at meal-times 'as a medicine rather than as a drink,' regarded sherry as preferable either to Rhenish or French wines, but he most approved of Canary: 'I have, during the fits of the last years, tried many things to lessen the symptoms. Nothing, however, effected my purpose so much as a small draught of Canary wine, taken now and then, when the faintness and sickness were most oppressive.' Neither the sherry nor the Canary wine of the present day has earned the approval of those who have tried them, though Canary is less gouty than madeira.

Claret of the best kind, and in good condition, is much less gouty than burgundy, and is decidedly the most useful wine for the generality of patients. Dry moselle is regarded by Sir Dyce Duckworth as preferable to Rhine wines, which are said to be detrimental.

Champagne is apt to be the worst of all wines in gout, but it has found in Dr. Mortimer Granville a strenuous supporter. Its effect on the gouty subject is largely a question of quality. Some of the inferior kinds combine almost every harmful peculiarity. Even the best are not entirely free from the disadvantages arising from an artificial process of manufacture. It is wiser for the gouty patient not to incur considerable risks by trying brands with which he is not familiar, though he may sometimes with impunity, and occasionally with benefit, enjoy a glass of a champagne which he can trust from personal experience.

With all wines quantity has a great share in determining the result. Even port wine is often tolerated if

the amount taken be sufficiently small. Many a patient finds himself the better for a glass or two of old port daily, and when this practice is not productive of appreciable harm, we need not interfere with its continuance. It is not, however, one which we could recommend for general adoption.

Ale and stout are strictly to be avoided. On this point the patients and the physician are in complete agreement. Ebstein\* forbids the use of beer on account of the carbohydrates which it contains, but thinks that wine need not be excluded if of the right kind, and taken in small quantities.

Cider is not open to the same objections as beer. In the districts in which it is largely consumed gout is not markedly prevalent. A distinction has, however, to be made between the sweet or imperfectly fermented and the rough cider. According to Sir Dyce Duckworth, who quotes Mr. Richard Davy's observations, the former is capable of provoking gout; the latter does not do so unless combined with gin, alcohol, or beer.

The notion that cider may dispel the gout is probably based upon the immunity enjoyed by those who make it their exclusive beverage. As pointed out by Duckworth, other factors co-operate with any influence it may possess: an open-air and laborious life, associated with free cutaneous action, such as that of Devonshire labourers, would probably be successful in curing many cases of goutiness. The consumption of cider at home without this saving clause would end in failure, if it did not at once lead to gastric or intestinal complications.

<sup>\*</sup> Ebstein (loc. cit., p. 167) quotes Mooren's observation that the acids of urine were least increased on Dortmund beer, much more increased by Rhine wine, more still by the choice kinds of moselle and old bordeaux, and most of all by the ordinary moselle.

### CHAPTER LXIII.

## HYGIENE AND PROPHYLAXIS IN GOUTINESS AND IN GOUT.

## HYGIENE IN CONNECTION WITH THE TREATMENT OF GOUT.

This is the age of hygiene. Much has been done for the prevention or cure of various diseases by attention to hygienic principles. Gout claims a large share of the same method; and its treatment, apart from the acute attacks, is mainly an adaptation of the laws of health to the peculiarities of the constitutional affection.

The section of hygiene specially concerned is not sanitation in the ordinary sense, which seeks to protect us from effluvia, from putrescible accumulations, and other dangers, but the internal sanitation which should regulate our supplies and dispose of our waste products. This object of treatment is in harmony with the pathological view which identifies gout with the faulty nutrition of an originally healthy organism.

The chief aspects of hygiene in gout relate to the influence of open air and of climate, of temperature and of the action of the skin, of muscular exercise, of mental activity, and of rest and sleep. The principle which should guide our management of diet, that of combining the greatest support to the system with the least fatigue to the functions, applies equally to this no less important branch of treatment.

### PROPHYLAXIS.

Prophylaxis, in the wider sense, is identical with perfect hygiene; its object is the prevention of gout in those strongly predisposed by heredity, and in others whom age, previous habits, and existing circumstances of life, expose to an obvious risk of acquiring the affection. The larger and most useful function of hygiene is the protection of the younger lives and of those of middle age who have not yet fallen victims to declared gout. The other function is corrective and palliative; its operations are, more or less, restricted by the general delicacy which they seek to remedy, or by the local changes induced by the chronic affection.

In the following remarks we shall not endeavour to sketch out with completeness the method of prophylaxis applicable in early life.\* Its principles do not widely differ from those suitable in general delicacy, unconnected with any gouty proclivity, and its special details may be inferred from those to be mentioned in dealing with the hygiene of gout and of goutiness.

The preventive treatment of the gouty attacks is a much more limited subject. Hygiene has a share in it; but its greater part is dietetic and medicinal. Prompt attention to any ominous indigestion or fit of dyspepsia, or to biliousness and constipation, is the essential therapeutical indication.

## THE OPEN-AIR CURE: OXYGEN, SUNLIGHT, AND RESPIRATORY THERAPEUTICS.

One of the chief objects in the selection of a climate for the gouty is to enable them to enjoy perpetually pure

<sup>\*</sup> The subject is referred to in an interesting work by Dr. Henry Cazalis, of Aix-les-Bains, 'Contribution à la Pathogénie de l'Arthritisme,' Paris, 1895, which contains a chapter on arthritism in childhood, and its prophylaxis.

open air—in the daytime out of doors, at night with widely open windows. Fresh air does good in proportion as patients can move about in it; and those merely threatened, or suffering from simple goutiness, will show the greatest improvement. The open-air method cannot cure stiff or distorted joints, but the solid though latent constitutional gain is to be valued the more where a relatively crippled state limits other treatment, and favours a progressive degeneracy.

Pure and bracing air is a remedy adapted to every stage and variety of gout; but it is of vital importance where there is a cachexia to check or to ward off. In cachectic patients detained indoors by unavoidable circumstances, systematic oxygen inhalations have been employed, and are of use, but they cannot compare with the natural supply of ozone and all its subtle influences.

Mechanical respiratory therapeutics have been too much neglected in this country as an essential part of the hygienic treatment of nutritional disorders. Some attention has been devoted to them in Sweden, and more recently in Germany. The cultivation of abdominal breathing has also been largely taken up by professional singers all over the world. Most forms of athletic pursuits doubtless fulfil, to a certain extent, the respiratory indication;\* but it is in those helpless conditions where, the mobility of the joints being impaired, active exercise is precluded, that full oxygenation is the most needed and

<sup>\*</sup> Dr. Edward Blake insists that athleticism does not in itself improve the breathing powers. He considers that some athletes are amongst the worst breathers; that proper respiration is an art in itself, and that it requires special training, without which athleticism may be most injurious. He urges that, by using the method he has devised, the athlete secures a considerable respiratory advantage with greatly increased muscular power. Cf. 'Constipation and Corpulency,' p. 13. Bale and Sons, 1893.

the least secured. Much, indeed, might be done by the patient himself, in spite of considerable limitation in the use of his limbs, by practising respiratory gymnastics, carefully selected with a view to his particular need.

Dr. Edward Blake, whose valuable contributions to the study of autotoxis are so well known, recommends a method\* which might be variously modified so as to be available in most instances. The practical advantages of his plan, as compared with mere routine massage, are obvious. In addition to an increased gaseous interchange, the active respiratory method supplies important requirements in the treatment of chronic gout: muscular exercise, mechanical stimulation, and movement of the abdominal viscera, more especially of the liver, of the portal system generally, and of the other abdominal veins. Much more oxygen is introduced into the blood, and the cardio-vascular system and the lymphatic circulation are favourably influenced to a degree scarcely to be equalled by any other method in the absence of active physical exercise.

It is probable that by these means a stimulation of the blood-corpuscle formation occurs, similar to that which has been recorded by so many independent observers, as following a change from a low-lying district to a lofty altitude.

Sunlight must now be recognised as an essential part of the climatic treatment. Sunlight and sunheat, as we previously felt, but are only now able to conceive, thanks to Röntgen's discovery, may strike through to the bone, and may perhaps visit the seat of gout in the joints. The sunlight cure has long been practised at Veldis with striking results, in connection with various disorders and debilities; but this object-lesson has been too little heeded in our hospitals, few of which possess the all-essential

<sup>\* &#</sup>x27;Lip Chorea,' p. 15 et seq. Bale and Sons, 1890."

sun-gallery. The influence of sunlight on health has been studied by various observers; among others, by Dr. R. H. Clarke and Dr. A. B. Blacker,\* by Dr. Samuel Rideal, F.C.S., and by Dr. Bowles.

The Veldis method comprises, besides the sun-bath and the open-air treatment, much in connection with diet and exercise, which would be of use to selected cases of goutiness. Short of the heroic practice of submitting an extensive cutaneous surface to the direct rays of the sun, much may be gained by a systematic enjoyment of the opportunities afforded in this country during summer, and all the year round in more sunny climates. This is one of the chief recommendations of the altitudes during the winter months. The intense radiation of sunlight and heat would be invaluable in many cases besides phthisis, and amongst others in gout.

### CLIMATE.

Little need be added to the remarks made under the heading of mineral springs. There are two climatic indications for the treatment of gout and of goutiness—warmth and a bracing air. In a few cases the condition of the digestion, of the mucous membranes, of the liver or of the kidneys, may need temporarily a soothing rather than a tonic influence. For the greater number a perpetual summer is the ideal climatic treatment, to which many attain by spending the winter at some distance from England. Others are content with the relative warmth of the South Coast; but in selecting between its resorts warmth will have to be considered rather than mere bracing quality. Brighton, which is largely patronized, combines both virtues. Abroad the winter colonies are also chiefly

<sup>\*</sup> Cf. Practitioner, vol. xlviii., 'Light as a Therapeutic Agent.'

to be found at seaside stations. Yet, although sea-air is preferred by some, it may be doubted whether in many cases a dry inland situation at a good altitude would not be more beneficial. In summer the Swiss Alps are largely resorted to with great benefit, and a visit to Switzerland is wisely recommended at many foreign balnear stations as a necessary complement of the cure. In winter the Alpine resorts are not suitable for chronic arthritic gout with fixation of joints. There are, however, cases of goutiness, of visceral gout, and even of gouty neuralgia, which would derive considerable benefit from a short winter season at St. Moritz during the months of January, February, and March. Age and inability for active exercise are absolute contra-indications. But among the younger and relatively active subjects there are many to whom the exhilarating effect of the dry and pure air, of the brightness of sky and of the intensity of solar radiation, and the invigorating effect of the long-continued frost, would prove of greater value than the merely protective virtues of the Mediterranean resorts.

Increased capacity for exercise is among the special recommendations of the Alpine treatment; and the respiratory indication to which we have referred is fulfilled unconsciously, owing to the great demands made by the rarefied air upon the respiratory muscles.

Although perspiration is not usually noticeable, the dryness of the air promotes insensible exhalation from the skin, and the cutaneous indication is not altogether neglected.

In spite of its many advantages, this tonic treatment is only suited to a limited number of subjects, and calls for judicious selection of cases.

Patients ready to submit to the more radical measure of a long residence in the altitudes, to an active open-air life, and to a diet chiefly of milk and of the vegetarian kind, are too exceptional to justify further reference to this treatment.

Among the winter resorts available and to be recommended for those able to travel should be mentioned Madeira and the Canary Islands. A trip to India or to the West Indies, to Australia or New Zealand, or to the South Californian resorts, will appeal only to the few.

### THE SKIN AND PERSPIRATION.

The hygiene of the skin, an essential part of the treatment of gout, has a twofold object: to strengthen the integument, and through it the nervous system and the entire economy, and to stimulate the excretory function and promote free cutaneous action. Cold or tepid affusions, sea-water baths or salt baths, friction, and massage, afford us a choice of tonic remedies, which will have to be varied according to individual requirements. These methods were practised by the ancients, and combined with the use of the hot bath and of the vapour bath. The latter are still our most valuable aids in promoting cutaneous excretion, which is the second indication. The Turkish bath is often resorted to with advantage. does not, however, possess absolute control over the gouty conditions. Sir A. Garrod states\* that he has known patients experience severe attacks of gout, although taking a Turkish bath almost every day. This fact is significant, and reminds us of the possible results which may, according to Sir W. Roberts, attend a sudden dehydration of the tissues and of the joints.

The immunity from gout peculiar to hot climates has been ascribed to the free action of the skin kept up

<sup>\*</sup> Loc. cit., p. 402.

continuously. Nevertheless, the protection afforded by perspiration is not sufficient to counteract the effect of habitual indulgence in animal food: this is well shown in the case of the Parsees in India.

The best form of perspiration for the relief of a gouty tendency is that arising from muscular exercise. Dr. Haig\* observes that the labouring man has summer with him all the year round, and gets rid of a large quantity of acid by perspiration in winter as well as during the warm weather. During the winter the sedentary man is more acid, because less relieved through the skin.

<sup>\*</sup> Loc. cit., p. 321.

### CHAPTER LXIV.

# MUSCULAR EXERCISE.—MENTAL WORK.— REST AND SLEEP.

MUSCULAR EXERCISE AS A PROPHYLACTIC AND AS A CURE.

The value of muscular exertion for the prevention and for the relief of gout was recognised by some of the earliest physicians known to history. Sydenham ascribes to its neglect a large share in the production of the affection: 'Add to this the intermission or sudden abandonment of those exercises to which from their youth upwards they have been accustomed. Whilst these were kept up the blood was invigorated, and the tone of the body rendered firm and steady. When, however, they were dropped, the animal spirits gave way, the frame lost tone, and the assimilation became imperfect. Hence the recrementitious portion of the juices of the body, which had hitherto been cleared off by the exercise in question, accumulated in the vessels and supplied the germ of the disease.'

His statements as to the curative value of exercise, even in tophaceous gout, are no less explicit: 'This is converted into a substance of the kind in question in the heat and pain of the joint; and it increases day by day, converting into its own proper substance both the skin and flesh. The deposit now lies bare, and it may be picked out. It has been compared to crab's eyes, chalk, and other similar matters. Now, this may be guarded against by daily exercise, whereby we obtain the due diffusion over the whole body of the humours that generate gout, instead of their accumulation in any particular part of it by preference. I have found in my own person that long and daily exercise not only stops the generation of chalkstones, but even dissolves old and hard ones already formed, provided only that they have not gone so far as to have converted the outer skin into their own proper substance.'

The importance attached to physical exercise by Sydenham could be illustrated by several other quotations; it is the more striking in contrast with his scepticism as to the use of physic. His ideas of the mechanism of the relief afforded are in complete harmony with modern speculations. If we are right in regarding gout as a perversion of the general metabolism of the body, the preponderance in weight of the muscular system over all other tissues would suggest that this must be the chief seat of the defect.

Dr. H. Cazalis,\* who regards 'arthritism' (an expression under which gout is also to be understood) as originally dependent upon an inherent weakness of the connective tissues, quotes some important views of Professor J. Renaut, attributing the excess in production of uric acid and of similar substances in gout to increased destructive changes in the connective tissues. This increased catabolism is, according to Professor Renaut, the result of an engorgement of the areolar system with waste products and with leucocytes loaded with uric acid and other effete materials. The engorgement is itself due to a failure of the muscles to keep up an efficient lymphatic circulation.†

\* Cf. loc. cit., p. 27 et seq.

<sup>†</sup> Renaut quotes Étienne Rollet's observation, that the relatively inactive gorilla is subject to chronic rheumatism, which does not affect the smaller and nimble species of monkeys.

The primary fault lies with the tendency of civilization to divert into nervous channels a great part of the energy intended by nature for muscular work.

Allowance being made for the facts and phraseology of modern science, we recognise in this latest utterance on gout the ideas of Sydenham. Muscular exercise is the means of preventing *lymphstasis* and all its consequences; and muscular inactivity leads to encumbrance of the lymphatics, and of the loose connective tissues, which latter Cazalis and Renaut regard as the great internal media of metabolic processes.

Upon the reaction of the blood muscular work is stated by Dr. Robert Hutchison\* to take a marked effect; it reduces the alkalinity of the plasma. Hutchison refers to the searching investigations of Cohnstein,† which place this result beyond doubt. The change was especially marked and lasting in the case of herbivora. Geppert and Zuntz‡ found in rabbits a reduction in alkalinity in the proportion of 146 to 248. Peiper,§ with the help of the titration method, was able to trace in man a reduction in the proportion of 182 to 218. Hutchison regards lactic acid as the agent, because, as experimentally proved by Spiro|| and by Werther,¶ this acid is always increased in the blood after muscular exercise. Sweat, not being normally acid, is not, in Dr. Hutchison's opinion, the channel through which acid is eliminated from the blood:

'The immediate fall in the excretion of urea' (which Dr. Haig has shown to follow exercise), 'is to be explained, in part at least, by the elimination of some of the

<sup>\*</sup> Cf. Lancet, April 25, 1896, vol. i, p. 1166.

<sup>†</sup> Cf. Virchow's 'Archiv.,' Bd. cxxx., p. 332, 1892.

<sup>‡</sup> Cf. Pflüger's 'Archiv.,' Bd. xlii., p. 233, 1889.

<sup>§</sup> Cf. Virchow's 'Archiv.,' Bd. cxvi., p. 337, 1889.

<sup>||</sup> Cf. Zeitschrift für Physiol. Chemie, Bd. i., 1878.

<sup>¶</sup> Cf. Pflüger's 'Archiv.,' Bd. xlvi., p. 63, 1890.

nitrogen which should appear as urea, in the form of compounds of ammonia, these ammonia compounds being required to neutralize the acids produced by the excessive muscular metabolism.'

Dr. Haig's latest views\* are at variance with those just quoted. He draws attention to the conflicting statements of authorities as to the reaction of sweat. Heuss† says that sweat is acid at the time of its discharge from the ducts.

A fall in the acidity of urine always, according to Haig, accompanies marked perspiration, whether this be procured by the Turkish bath or by muscular exertion; and conversely, as pointed out by Garrod, suppression of perspiration causes a rise in the acidity.

The fall of urea which exercise may produce, and the associated fatigue, can both be prevented by controlling the uric acid.‡ Though, as shown by Auerbach,§ carnivora possess the power of forming ammonia to neutralize acids, that power is ill developed in man and the frugivora, and this is regarded by Haig as probably accounting for the very different reactions of their urines, and as supporting the argument that man is not by nature a carnivore.

Whatever view be taken of the chemistry of muscle and of sweat, the broad practical conclusions are obvious.

Gout is usually acquired at an age when the vital processes are slackening speed, the body-weight is increasing by the deposition of fat, and, owing to many occupations, or sometimes to indolence, muscular exercise has been more and more sacrificed. Gout eventually results; but it has often been long preceded by a falling off in hygiene. In

<sup>\*</sup> Cf. Lancet, May 2, 1896, p. 1250.

<sup>+</sup> Monatsch. für Prakt. Dermat., No. 9, 1892.

<sup>‡</sup> Cf. Haig, Lancet, March 7, 1896, p. 614.

<sup>§</sup> Virchow's 'Archiv.,' vol. xcviii., p. 512.

this country a neglect of the muscular function in middleage is probably resented in proportion to the prevalent muscular activity of earlier life.

Our lives are often ill managed in this respect. Up to the age of thirty our muscles are always ready for almost any call, however long the intervals of rest. Between thirty and forty this readiness is rapidly lessening; but too often the gradual change is overlooked till it is almost past recovery. At this stage distinctions are established between men by temperament, by build, and by occupation. The lean, active, and hard-worked toilers suffer least; but the fat, prosperous, and indolent can no longer keep pace with them.

If the inevitable results could be foreseen in time, whilst all works smoothly still and without effort, nothing would be easier than to maintain physical activity by regular exercise. Past a certain age, the strenuous effort to recover lost ground is in itself a risk.

Most men ignore the fact that with growing age muscular efficiency is more and more a matter of constant study. It can only be kept up by unceasing practice. Left to themselves, the organic activities follow their downward course. Each day marks a relative loss of fitness, unless the renovating influence be daily applied.

It is not only the muscles, their nutrition, suppleness, and power, which are in question. The mainspring lies in the heart and in the pulmonary function, without which muscular activity is impossible. The right side of the heart and the lungs have to be kept in training, as the indispensable auxiliaries to the muscular system, by systematic regularity in exercise.

The prevailing custom of taking full exercise once a week, leaving the other days unprovided for, works well enough for the young, though the intermissions may be most

keenly felt by them. After the age of thirty some form of daily exercise should be selected and adhered to; and the choice is now varied.

Horse exercise, of which Sydenham held that it was of so much value in gout that, had it not been long invented, its inventor might have realized a fortune, is still unsurpassed; but the bicycle now throws analogous, and sometimes superior, advantages within the reach of the larger number. The more sedate, if heavier, tricycle has long been the secret of health for many a gouty subject physically unfit for equitation. A sharp walk up-hill may suffice to cause the skin to act, but mere walking, especially on level ground, fails to 'shake the liver.' This is one of the boons of riding a horse or a tricycle. The mechanical jolting of the viscera is brought about passively and without additional effort; whilst the active methods of securing this result, even the use of the skipping-rope, entail more exertion than many could attempt.

All open-air exercises are much to be preferred to the various forms of gymnastics devised for home use; in addition to their exhilarating effect upon the nervous system, they possess the higher oxygenating value attaching to rapid movement through space. Chamber gymnastics offer, however, many advantages; they can be varied so as to suit almost every degree of debility or of articular affection; they save time; they are independent of the weather; and they may be religiously performed as part of the toilet, with every facility at hand for the warm sponging and cold affusion which are the proper complement of all forms of exercise accompanied with sweating. At any rate, any advantage gained may be kept up in this way, so as to minimize the risk of a gouty attack being set up by some unusual physical exertion. Fortified by this daily allowance of work, gouty subjects will derive greater benefit from a periodical visit to Angelo's or to any of the fencing-schools for an assault with foils or a bout with single-sticks, from a round at the links, or, if enjoying the advantage of residence in the country, from frequent outings with rod or gun, or from the varied outdoor pursuits of a country life.

### THE HYGIENE OF THE FOOT.

Little, probably, can be done by local measures to obviate the tendency to a localization of the gouty inflammation in the toe and in other joints. Yet some attempt might be made, with that view, to place the threatened joint under the most favourable conditions.

In ordinary life the movements of the great toe are always much restricted by boots or shoes; and too often injurious pressure is exerted upon it, and upon other parts of the foot. Both these evils should be met. Passive movement and massage to the joints of the foot, and particularly to that of the great toe, would fulfil the first indication; and this forms part of the treatment at some of the mineral springs. Walking barefooted or in socks, and active movements of the toes when the foot is free and at rest, are also obvious means of improving the lymphatic circulation in the fibrous structures, and of strengthening the joint.

It would be equally rash to assert that the gouty inflammation was provoked by the pressure of ill-fitting boots, and to entirely exclude that influence from its ætiology. Our obvious duty is to warn those predisposed to gout against this source of danger. In the children of gouty parents the jealous watchfulness exercised during infancy over the beautiful symmetry of the foot should not be suspended, as too often happens, during later childhood, or with the advent of puberty, when an unintelligent vanity too often begins its destructive work; and vigilant attention should be bestowed upon the timely supply of well-made and hygienic boots or shoes, to meet the recurring needs of the growing foot. As the gouty age approaches, increasing care should be given to these important details.

### MENTAL WORK AND MORAL INFLUENCES.

The efficacy of excessive mental application, of moral shock, and of mental depression, in exciting a fit of the gout in those who are confirmed sufferers, is well authenticated. It may be doubted, however, whether a tendency to gout can be materially increased by mental labour in itself, though Sydenham's authority has given it a bad name: 'The same mischief follows the over-application of the mind to serious matters and deep study. Melancholy, so called, is pre-eminently the inseparable companion of gout. Hence those who are liable to it are so wont to tire and overwhelm the animal spirits by long and deep thought, that excessive exertion of this sort, even without the artificial aid of reading, makes the proper preservation of the economy of the body an impossibility; for which reason (as seems to me) gout rarely attacks fools. Those who choose may except the present writer.'

A sharp distinction should be drawn between healthy mental activity and the excessive and exclusive strain which is too often thrown upon the mental powers. This, like every other exhausting influence, favours the onset of the paroxysm, and like any other cause interfering with the due exercise of the muscular functions, it must tend, if other circumstances should co-operate, to develop gout in those previously free from it.

Neither physiology nor common experience warrant us in regarding mental activity and vigorous cerebral work in any other light than that of a tonic and vitalizing influence. Amongst the most active and assiduous brainworkers we find numerous cases of longevity, and commonly the most healthy lives. These are almost invariably instances of men who have known how to vary their labours. We may repeat that the best rest for brain fatigue is muscular exertion. Within the limits of individual strength both functions are conducive to health and longevity, and both are beneficial from the point of view of gout: but they must be wisely combined. If the essential requirement of muscular activity is not neglected, we agree with the late Professor Cantani's opinion, that mental work, free from worry, is good hygiene, even for those who may be gouty or predisposed to gout.

### REST AND SLEEP IN THE DAY.

The last of our duties is one of primary importance. It is, together with food, the foundation of the hygienic treatment of gout by exercise.

Rest in the horizontal position is, in all states of debility, and especially at the gouty age, the indispensable adjunct of active muscular exertion. The latter can only do good on the condition that the cardiac energy is economized. The heart will gain power in proportion to the additional rest to which it is entitled by hard work. The allowance of rest must be at first liberal, and the amount of exertion very gradually increased. When the heart and the muscles have been trained to efficiency by careful management, a few minutes' reclining at full length will often suffice to restore the feeling of freshness which indicates a return of full systolic adequacy.

A neglect of this saving clause of rest for the heart explains the failures and the damage too often observed as a result of a good method, badly applied. Independently of any systematic exercise, mid-day rest is often needed by overworked subjects, and the best time for taking it is immediately before the mid-day meal or the afternoon tea. A useful instalment of cardiac rest is also gained by men of sedentary occupations by making a practice of sitting when at work with the feet and legs supported in the horizontal position.

### SLEEP AND REST IN BED.

Long hours in bed are undesirable in chronic gout or goutiness, tending to relax when stimulation is wanted, and to encourage the habit of dozing, which may destroy the aptitude for sound sleep. The boon of deep sleep is one to be jealously guarded. Tea and coffee should, for that reason, be avoided by most patients after five o'clock in the afternoon. The best sleep is not always that which lasts the longest—quality making up for a less duration. Adequate exertion during the day is the means to secure it. The hours of sleep should not, however, be stinted: at least seven hours are necessary; an eight hours' sleep is ample, and this allowance should not usually be exceeded.

Insomnia, the prevailing cause of which is dyspepsia, may also be induced by the wilful neglect of hygiene. The habit of sleep is capable of cultivation, but it may easily be lost by over-fatigue of the brain and late hours. Again, insomnia may be brought about by excessive indulgence in morning slumbers. A rigid rule of early rising soon restores in these cases the capacity for sound sleep.

Early risers need a brief period of sleep in the day. It should be obtained, if possible, before lunch. The indulgence in a long sleep after meals is strongly deprecated in most

conditions, but particularly in gout. The habit of relative activity after meals, though irksome to acquire, and not suited to all, tends to strengthen the digestion, and to safeguard the night's sleep.

Sydenham insisted much on the virtues of early hours: 'Next to bleeding and purging, nothing undermines the forces of Nature like late hours. . . . Hence I advise gouty patients, especially in winter, to go to bed very early, and to rise betimes, however much their shortened slumbers may induce them to seek a morning's sleep by lying in bed, the more so as every morning slumber subtracts so much from the next night's rest, and so does violence to Nature. Perversely to turn day into night, and night into day, is to despise her prudent economy.'

We need not follow Sydenham in a discussion of the relative value of sleep taken early or late in the course of the night whilst its duration remains the same—a subject much complicated in modern times by the introduction of gas and of electric light. Dialectics, in the endless discussions on this topic, will never prevail against the rules of common-sense. Health, which early hours invariably promote, is wealth in itself; it may also mean wisdom, bearing out the spirit, if not the letter, of the proverb.

#### HABIT AND CHANGE.

'Chronic diseases, always excepting those which arise from internal agencies or inherited defects, are in the main dependent upon violations of physiological laws.' 'Return to the ways of physiological righteousness, and you will be healed.'

These words of Sir Andrew Clark apply with special fitness to acquired gout, which illustrates the *influence of habit* in its mode of production and in the method of its

cure. The late changes induced by inveterate gout are most often incurable; but in its slighter degrees, and before the advent of senility, gout is sometimes cured, and it is always capable of alleviation. The first requisite is to put a stop to the faulty habits, which by long continuance have warped the normal play of functions. Freed from this pressure, the vis medicatrix natura reasserts itself, and an upward tendency is established. But hygiene can do more than merely secure the conditions which least hamper Nature. Her constructive energies must be aided by the slow, but steady, influence of hygienic habits. Their action becomes cumulative if kept up. Health must be made a constant study, and those habits should, if possible, be acquired which are conducive to vitality. Reform cannot be introduced without some effort; but it becomes less laborious by practice, and brings with it increasing capacity for enjoyment and chances of longevity. If life is harder, faster, keener than it was, yet for toil or for pleasure it is perhaps felt better worth living than ever before, and will amply repay the cost.

Strict observance of the rules of hygiene is made easy if they should include sufficient variety. Monotony is depressing. The stimulating virtue of change is perhaps nowhere more apparent than in connection with gout. Our most potent hygienic stimulants, change of air and of scenery, are always combined with a break in the routine of life; and no other measure can in this respect compare with foreign travel. The same principle might, however, be applied in many other ways. The renovating influence of change should never be lost sight of, and should be provided as far as possible in the regulation of every-day life.

This applies to the majority of cases, but in respect of

change and of variety, as in everything else in gout, one great principle governs all others. Allowance must be made for peculiarities of circumstances and of disposition. The proper treatment of gout is to treat the patient. Whether in respect of diet, or of stimulants, or in connection with exercise and change, no rigid rule can be laid down for general application, and purely theoretical views should always give way to the practical indications of the individual case.

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FINIS.

### ERRATA.

For "Chemotaxis," pp. 108, 150, 288, read "Chemiotaxis.", "Veldis," pp. 563, 564, read "Veldes."









