Johan Schioldann: History of the Introduction of Lithium into

Medicine and Psychiatry

Birth of Modern Psychopharmacology 1949

Part I

Birth of lithium therapy 1859

Chapter 2. The concepts of recurrent gouty mania, recurrent melancholy & gouty insanity. Auto-intoxication

The notion that recurrent gout could cause both gouty mania and gouty melancholy was carried over into the nineteenth century. From this time a considerable number of psychiatric and medical textbooks contained often rather detailed descriptions of the protean manifestations of gout and their treatments.

A scrutiny of some these invaluable and fascinating sources reveals that gout was assumed to be intimately connected with disturbances of the nervous system. These often took the form of gouty insanity—especially in the form of either gouty mania or gouty melancholia without a predictable course or outcome, other than the alternating, recurrent pattern of articular and abarticular ('irregular') gout.

It is against this historical background that the origins of lithium treatment must be considered.

A most fascinating description of 'violent' gouty insanity and gouty melancholia as they were observed in the late 1700s and the early 1800s (and later referred to by Maudsley), is found in Arnold's famous Observations on the Nature, Kinds, Causes, and Prevention of Insanity:⁷⁰

In the cases of gout, erysipelas, herpes, or cutaneous eruptions of various kinds, whose repulsion, and translation to the brain, are reckoned in the table [see Arnold's book The Remote Causes of Insanity, pp.6–11], among the causes of insanity, it is taken for granted, that there is no discharge suppressed; or none of sufficient moment to produce a plethoric state, or otherwise to excite any material disturbance in the animal economy. Their repulsion appears capable, however, of giving occasion to insanity, either by disordering the system in general, and the first passages in particular; and producing indigestion, preternatural irritability, uneasy sensations, diminished tones, languor, and dejection; and affecting the brain in

⁷⁰ Arnold T.: 'Observations on nature, kinds, causes, and prevention of insanity. In two volumes. Vol. II. Containing observations on the causes and prevention of insanity' [1786]. 2nd Edn. London, 1806. pp.154—156. (Reprint. New York: Arnold Press, 1976). Nothing of relevance in this context was mentioned by W. Pargeter in his 'Observations on maniacal disorders', London & Oxford, 1792 (reprinted by Routledge, 1988).

consequence of these disorders first excited in the alimentary canal, in the tones, in the state of irritability, and in the feelings; or by directly attacking the brain, and producing sudden, and violent insanity, by suddenly increasing the action of its capillary vessels, and thus giving rise to a sudden accumulation of blood in the head, and a violent and disorderly excitement of the nervous energy, and of the functions on whose due procedure the sound and orderly state of reason, imagination, and the affections depend.

Melancholy, we are told by Sydenham is the almost inseparable companion of the gout [p.467]: and it is well known that ingestion, and all the consequences of a debilitated, and irritable state of the first passages, are its very common attendants; and as it is so often in a wandering, and unsettled state, and may fix in almost any part of the body; it is easy to conceive that it may produce insanity in both these ways.

But it must be acknowledged, with regard to some of the supposed translations, whether of the gout, erysipelas, herpes, or other cutaneous eruptions, it may be questioned whether the insanity be not the cause of the repulsion, or disappearance of the disorder; rather than its translation to the brain the cause of the insanity. And the same may be said of many supposed instances of disordered mind from suppressed evacuations. Dr. [Richard] Mead ('Medical Precepts and Cautions; Chap. iii. Works, vol. iii. p.42–44')⁷¹ has observed that insanity not only preserves the patient from other diseases, but when it seizes him actually labouring under them, lays such strong claim to the whole man, that it sometimes dispossesses the body of them: and relates a case of a dropsy cured, and of a consumption stopped for a time, by coming on of insanity. I have frequently seen instances of it succeeding most of the causes enumerated under this article; have often met with it in persons subject to regular fits of the gout, who have not had the smallest appearance of their usual gouty paroxysms during very long periods of this disorder: and I have known a case in which an habitual asthma entirely disappeared during more than one fit of insanity, and returned as usual when the insanity ceased.

Another fascinating case vignette describing the 'nervous' manifestations of gout is found in Perfect's *Annals of Insanity*:⁷²

A. M. a gentleman of fortune, habitually intemperate in his way of living, subject to regular fits of the gout, and to an hereditary asthma of the humoral kind, having had no return of arthritic affection for nearly two years, became suddenly low-spirited, with great distress and anxiety of mind; every trifling occurrence was considered by him as an object of intense trouble and inquietude, he was disgusted with almost every thing and every body, and entirely rejected those enjoyments and relaxations of life that had before given him the greatest pleasure and satisfaction; and in a short time, his mind was sunk into the lowest abyss of melancholy and dejection.

It is extraordinary, that from the very commencement of mental derangement, he was totally exempt from the asthmatic complaint, and

continued so from the beginning of February 1785 till the latter end of November following, when he complained of drowsiness, languor, and dullness, attended with rigors and sickness; and soon after was attacked with pains in his feet, ankles, and the calves of his legs; when in a few hours he became as clear in his imagination and senses as ever he had been in his life, and continued so throughout the whole gouty period of almost nine weeks; during which interval the asthmatic disorder, as he became insane, receded, as it had done before. He now expressed the most violent resentment against his nearest relations, was mischievous in his designs against himself, and would certainly have committed suicide had he not been carefully prevented. This he continued under the influence of the most desperate insanity, until the latter end of the following April, when he was seized with a shivering, and slight fever, that was succeeded by a regular fit of the gout, exempt from the asthmatic complaint, which was attended with the same intellectual clearness and perspicuity as before, and again recurred upon the declension of the gouty paroxysm, which again left him a prey to the ravages of mental derangement, and asthmatic affections.

In this state he was removed from my care; and the last information I heard concerning him was that he had experienced no return of the gout during a period of twelve months, that his lungs were in a very weak state, attended with a wasting of every part of his body, indicative of a general decay; and that soon after he was attacked with a gouty dysentery, which terminated in an abscess of the bowels, and occasioned his death.

Trotter's well-known 1807 treatise, A View of the Nervous Temperament, was 'a practical enquiry into the increasing prevalence, prevention, and treatment of those diseases commonly called nervous, bilious, stomach and liver complaints; indigestion; low spirits; gout, &c.':⁷³

How far the class of nervous diseases is connected with gout, may perhaps, require much future experience to determine. But as far as the inflammatory symptoms are not concerned, the two affections appear to be the same. They both depend on hereditary or acquired predisposition: the causes which produce them are entirely alike: these are chiefly luxurious habits and debilitating pleasures: all the dyspeptic ailments of the nervous frame, appear in the arthritic constitution. Every derangement of the biliary secretions, partakes in each, of a similar disposition; the state of the intestinal canal is subject to the like capricious vicissitudes in both; and also the urinary organs. The irritable feelings, and hallucinations of mind, with which both subjects are affected, have an exact resemblance. And we observe, that the prevention and treatment of nervous indisposition and gout, are to be conducted on the same principle.

No fact in medicine appears more clear, than that the female of every gouty family inherits in a high degree, the nervous temperament.

Pinel gave the topic consideration in his epochal Traité Médico-Philosophiques Sur L'Aliénation Mentale⁷⁴ to the effect that

L'observation la plus constante apprend en effet que la manie, l'idiotism, la mélancolie, la démence, peuvent également résulter d'un coup sur la tête, de la suppression d'une hémorrhagie, de la rétrocession de la goutte à l'intérieur, etc.

Pinel's student, Bayle,⁷⁵ reported cases where 'le rhumatisme avait présenté des dérangemens plus ou moins considérables, ou même s'était entièrement supprimé depuis longtemps, lorsque les premiers symptômes de méningite chronique se manifestèrent'. He made reference to a patient in whom 'l'aliénation succéda à des douleurs rhumatismales et goutteuses, qui existaient depuis longtemps et revenaient assez fréquemment'.

Esquirol in his equally epochal Des Maladies Mentales⁷⁶ espoused the view that la folie could be caused by 'la rétrocession de la gale, des dartres, de la goutte, des rhumatismes'. He took up the issue debated by several authors as to whether gout was a primary or secondary cerebral condition. In his opinion, 'la suppression' of these gouty conditions is not always 'la cause de la folie', but generally precedes its invasion.

At the same time, Reydellet⁷⁷ recounted that 'les auteurs sont remplis d'exemples de manie et autres aberrations des facultés mentales, déterminées par cette métastase', i.e. gout.

Similar views are found in Italian medicine. Bufalini⁷⁸ in 1833, summarising several authors on the subject, also professed to a linkage between 'la diatesi urica', 'la soprabbondanza dell'acido urico', and the 'constituzioni nervose ed irritabile [...] Il temperamento sanguigno ['e bilioso']', is prone to 'affezioni reumatiche', 'i tumulti reumatici' and 'moltiformi affezioni nervose'. Finally he made reference to Landré-Beauvais's 1800 treatise on [la] goutte asténique primaire. This author discussed whether 'une nouvelle espèce de goutte sous la dénomination de goutte asthénique primitive' should be given consideration.

Ellis,⁷⁹ in his 1838 treatise on insanity, expressed a cautionary note as to the generally assumed psychiatric manifestations of gout. He said that though it 'has been classed by many authors as a cause of insanity, [it] is of such rare occurrence amongst the poor, that very few cases from this source have fallen under my notice. We have not had one instance where, as far as we could ascertain, gout has been the cause of insanity'. But on the other hand, Ellis had 'no doubt that if it, or any other disease, be suddenly repelled, it will, in some constitutions, fly to the brain'.

According to Morel, at a meeting at Société médicale des hôpitaux de Paris, in 1853, Vigla reported six observations of 'rhumatismes articulaires suivis d'un délire plus ou moins prolongé et violent', followed by a discussion as to frequency, production, symptomatology, development, and various forms of this condition. 80

Subsequently, Gilbrin devoted a doctoral dissertation to the subject of uric acid diathesis,⁸¹ presented in 1858. He concluded that 'la diathèse urique porte aussi son action sur le système nerveux' in support of the view that it could cause conditions such as 'des apoplexies nerveuses, des vertiges, de l'hypochondrie, de la manie, du délire'.

Berthier⁸² of Bicêtre in his De la Folie Diathésique, published in 1859, recorded that a lady predisposed to 'de longs chagrins' developed pains in the smaller joints of the hands. These gradually ceased followed by 'un accès violent de manie'. As this went into remission, the pains recurred. Another lady was 'prise d'agitation maniaque', alternating with podagra.

The view that both depression and exaltation could be manifestations of gout was eloquently expressed by the widely read Trousseau⁸³ in his 1861 *Clinique Médicale de l'Hôtel Dieu de Paris*. The New Sydenham Society published it in English translation ten years later:

The most prominent premonitory symptoms of an attack of gout are disturbances of the nervous system. The gouty subject, at this period of his attack, complains of weight in the head, and inaptitude for every kind of intellectual labour: the altered cerebral condition is indicated principally by a nervous excitability which is often excessive both in regular and irregular gout, but particularly in the latter. This nervous excitability shows itself by phenomena varying much in their character according to the individual. There is an undefinable character of discomfort, and mental uneasiness; and curious changes of disposition. Though some persons show an exaltation of their brilliant qualities, this is far from being always the case. Gouty persons generally acquire a morose, susceptible and irascible temper, formerly foreign to them. This is so usual that it has passed into a proverb with authors on gout. So great, sometimes, is this perversion of disposition, and so constant is it in some persons, that not only the individuals themselves know that an attack is coming on, by feeling causelessly cross for some days, but also those about them can foretell the attack by these moral phenomena; just as the catamenial period is announced in some women by a manifestation of changes in the mental condition.

Dagonet⁸⁴ recorded in 1862 that one of his patients suffered alternately from attacks of gout and mental disorder.

The issue of gout and insanity soon became a much debated topic in medical societies.

Legrand du Saulle in *Société Médico-Psychologique* at Paris in 1862 raised the issue of the possible 'alternance' between 'les accès de folie et les crises arthritiques'. 85 de Cailleux wished to call to attention that he had observed two cases with such a 'coexistence de la goutte et de l'aliénation mentale, notamment chez une religieuse affectée de mélancolie'. Loiseau had encountered a couple of cases, in one of which 'l'aliénation était venue remplacer des accès de goutte pénibles et fréquents'. Delasiauve remarked that it was a question of practical interest. He had observed a case where 'une sorte d'agitation

lypémaniaque alternait avec les symptômes arthritiques'. Finally, he thought that 'un travail sur ce point mènerait à d'inévitables résultats'!

This challenge was taken up by Berthier. In 1869 he could publish his review, ⁸⁶ De la folie goutteuse, based on twenty-two cases of various types of mental disorder ascribed to gout, reported by different authors (including himself); some of them were referred to above.

Concerned that the 'long known' dependence of 'nervous derangement' upon a 'gouty habit' had not been fully recognised, Reynolds⁸⁷ raised the issue at the British Medical Association:

Many cases have come before me in which there was great restlessness; the patient could not be still for a moment; was alternately excited and depressed; slept badly, or not at all; was intensely hysterical; and could not attend to business; while others have complained of failing memory; of want of power of attention; of suicidal thoughts; of intense melancholy; others of sounds in the ears; voices, sometimes distinct, sometimes not; and some or all of these of long continuance.

Gouty melancholia was also discussed in the columns of the Journal of Mental Science (the forerunner of British Journal of Psychiatry), for instance by Clark⁸⁸ in 1880:

- 'Well, doctor, what do you think is the matter with my patient?'
- 'I think it is a case of gouty melancholia'.
- 'Gouty melancholia! Ah!'
- 'You seem surprised and incredulous.'
- 'No, doctor, I was just thinking that the last two or three cases which I brought to you turned out to be gouty, and I was wondering what "gouty" really meant'.
- 'What it exactly means to other people I do not pretend to know; what it means to me I can tell you very shortly. Your patient is in what I call the gouty state, and by the gouty state I mean the state brought about in certain constitutions by the retention in the blood and tissues of the body of certain acid and other waste stuffs, and their effects thereon'.

After having expanded on his views to the incredulous colleague, a case was discussed:

- 'Now, doctor, kindly show me how you apply these views to the case of my patient. How do you make out that his trouble is, as you have called it, a gouty and not an ordinary melancholia?'
- 'Well, as you admit the existence of the melancholia, we need not dwell longer upon that [...] Four years ago your patient was suffering from indigestion. He was nervous, irritable depressed, sleepless, full of fears.

He had little liver attacks, when his urine became dark [...] He got sometimes better, sometimes worse, but never well. And suddenly, in the cold spring, you remember, he had a slight attack of gout in the foot. After this he was well for two years, living carefully [...] At the end of this period [...] his hygienic zeal having abated, he again fell into a state like that from which he had escaped through his attack of gout. Again gout made him well. Again, having fallen into loose ways of eating and drinking, and neglected every form of exercise, he drifted, a few months ago, in the cold spring, into the old state. He became dyspeptic, flatulent, acid, his bowels were irregular, his urine light coloured and low in density [...] He has recurring headaches [...] he is irritable, nervous, depressed, sleepless, full of baseless fears, and he suffers on waking from a seemingly causeless agony, which subsides as the day advances [sic]. Here, in an aggravated degree, is the assemblage of symptoms which, before, were immediately and completely relieved by an attack of gout. But now there is no gout, and so, as I think, the symptoms remain. So the gouty stuffs retained in the blood and in the tissues strike with a partial severity the nutritive and functional activities of the nervous system, and you have the melancholia as the substitution for the gout. This is your patient's gouty melancholia'.

Still in 1880, similar views were expressed by Duckworth in his 'plea for the neurotic theory of gout'. 89 He spoke of 'a special toxaemia', 'the effects of the blood-dyscrasia upon the nerve-centres', 'a diathetic neurosis'.

'The influence of many of the existing causes of gouty paroxysms', he went on to state,

illustrates well the explosive character of the malady. As Sydenham expressed it, before the onset of an attack, 'totum corpus est podagra'. The precipitation of the seizure sometimes ensues almost immediately upon the provoking cause. In a large number of instances, the latter is of a nature to depress nervous power [...] Irritability of temper is a proverbial condition in the gouty, and furious outbursts of this kind appear to be, at times, a metamorphic substitution for a more overt and regular attack. It is important to know that many of the minor, but none the less well-marked, phases of gouty paroxysm are in no degree arthropathic. Much error in diagnosis has arisen from taking no heed of any but articular symptoms when searching for gouty tokens in a given case. These less classical attacks very commonly precede the onset of typical ones at a later period in life.

The necessity for prompt recognition of these less well-expressed symptoms is obvious, if good treatment is to be applied.

Significantly, Duckworth also mentioned that 'Epilepsy has been known to disappear on the supervention of gout'.

The following year, in 1881, he reiterated his views on gout considered as a trophy-neurosis:⁹⁰

A consideration of the mental condition of the goutily disposed throws light upon the nervous pathology of the malady. Intense irritability of temper is proverbial, and an outburst of rage is sometimes a metamorphic substitution for a regular attack of gout. Hypochondriasis, low spirits, and grievous forebodings, sometimes give token of the approach of gout.

In the history of the generally presumed psychiatric manifestations of gouty diathesis it is important to note that gouty insanity was debated at some length at the 1881 International Medical Congress held in London. The Congress attracted doctors from around the world, including America and Australia.

Rayner⁹¹ of Hanwell Asylum, Middlesex, read the paper Gouty Insanity, asserting his belief that, although proper statistics were lacking, 'gout is as frequent a cause of insanity as of any other disease'. He referred to Berthier⁹² who, in his opinion, 'seems to have been the first [in 1869] to collect the recorded cases of insanity from gout, which proved (what I had previously concluded) that any form of insanity may be thus produced'. He wished to support Berthier's views and demonstrate how gout seems to produce insanity. He turned his attention to the 'retrocession' of gout being frequently observed to produce insanity, most commonly mania, 'very sudden in its inset, and rarely lasting long, recovery being ushered in by an attack of gout'. He also paid attention to the 'atonic' form of gout where 'the symptoms [are] hallucinations of sight and hearing, producing great suspicion and distrust; the patients recovering after an attack of gout'. Finally, he mentioned 'restrained' or 'in-pent' gout, which he illustrated with a case where 'delusions were at first exalted; these were soon followed by a state of melancholy, which disappeared after an acute attack of gout consequent upon great improvement in health'.

Savage, superintendent of the famous Bethlam Hospital in London, very influential in British psychiatry and, according to his obituarist Smith, 93 well acquainted with the international literature, had been in attendance. In the ensuing discussion, 94 Savage expressed himself 'as a convert to the belief in gout as a cause of insanity'. Crichton-Browne voiced the opinion that 'insanity only occurred in gouty patients who were hereditarily predisposed to insanity or epilepsy, when the nervous disturbance produced may pass on into actual insanity'. 95

These discussions were later reported in 'Notes and News' of the *Journal of Mental Science*, according to which Savage had expressed the view that ⁹⁶

they certainly did find cases of insanity associated with so-called suppressed gout. Gout really did cause a considerable amount of insanity; but then they wanted a definition of gout. Here and there they got cases which scarcely required definition. A short time back a patient was admitted into Bethlem who had been a free-living man, and had both inherited gout and developed it. He had melancholia, and was suicidal. That man was for months a cause of the utmost anxiety. One day (Dr. Savage said) on going his rounds he saw the patient resting his foot upon the chair, and he said, 'It is all right now, sir'. He had got an attack of gout, and he was well. He (Dr. Savage) had

constantly heard the same thing in relation to people suffering from suppressed gout. He had some doubt about the relationships of neuroses and gout. However, these cases required further investigation.

Fascinatingly, according to the same source, Crichton-Browne, similar to Ellis, argued that there was 'no necessary or essential connection between gout and insanity, because there were many thousands of gouty people who never manifested mental disorder'. However, he also conceded that sometimes

gout seemed to mount into absolute mental derangement. It did so, for instance, during the pyrexia of gout, from the protracted pain, which the patient suffered. He thought that the gouty tendency often mounted into insanity in the male in the climacteric period—about fifty or sixty in men; and these cases were sometimes cured by an acute attack of gout taking place.

Bruce⁹⁷ 'had called attention to the connection of gout with the physical symptoms accompanying attonic melancholia, and had no doubt whatever that they were associated with inherited gout'.

Savage, somewhat vacillating in his view as to a relationship between gouty conditions and mental disorders, in his standard textbook Insanity and Allied Neuroses⁹⁸ could not 'clearly point out [...] the connecting link' between gout and insanity. However, he stated that

at present we have only to consider that occasionally an attack of insanity seems to replace an attack of gout, and that an attack of gout may take the place of insane symptoms. [Moreover], it is noteworthy that in some cases in which a gouty patient has become suddenly melancholic, the attack may come on quite suddenly, and quite early in the morning, so that a patient who has been liable to recurrence of gout is found intensely depressed on a certain morning, and from that time remains deluded and suicidal, no change occurs till, some morning early, he has an attack of gout, when all depression of mind passes away.

Savage went on to illustrate this with the intriguing case of John E., a naval officer, fifty-three years of age, who had been admitted to Bethlem Hospital under his care with 'so-called suppressed gout'. It was probably the case cited previously, and is quoted here from an excerpt that he published in Tuke's Dictionary of Psychological Medicine:⁹⁹

[John E.] after many years of gout, suddenly developed the most intensely suicidal melancholia. He made repeated attacks on his own life, and when in Bethlem was considered to be one of the most suicidal and dangerous patients we had. Constant care and watching were required to prevent him effecting his purpose. This continued for some months, till one morning in going round the wards we were pleased and astonished to hear the patient's voice in a cheerful way saying 'Good morning'. We noticed that his foot was raised, and wrapped in wadding, and he told us it was 'all right now', as he had got 'his old friend back', and 'please God I'll never lose it if I can help it'.

Savage also described 'other varieties of gouty disorder which deserve consideration', 100

but which are not directly connected, as far as we know, with any alternation, except, that instead of fully developed gout, one meets with cases of mental depression occurring in gouty subjects which follow a more or less definite course; this the depression is most marked in the very early morning, and persists until mid-day, when it slowly becomes less, and by six or seven o'clock has all but passed off, and during the evening no one would suppose that the patient had been intensely melancholy in the early morning.

'These cycles of depression', which from a modern viewpoint appear identical to manifestations of endogenous depression with terminal insomnia, diurnal variation and evening remission; or, in Savage's words, they 'recur and recur with pretty regular precision unless treated from a gouty point of view'. Savage provided no further particulars other than to mention 'Turkish baths, saline purgatives, and change of surroundings'.

Concerning the fact that attacks of 'acute mania' had been described as 'depending on undeveloped gout, and as passing off with the development of acute gout', Savage had not seen such a case himself.

If Savage had not himself observed hypomania or mania to occur in gout, he might not have doubted their presumed occurrence had he consulted Milner Fothergill's well-known The Heart and its Diseases. ¹⁰¹

Fothergill had been 'completely baffled' by this condition until he came across Bence Jones's Physiological Essays, 102 where he found it described. He 'was struck with the occasional irritability, active and positive, manifested in the subjects' suffering with chronic kidney disease, and he came to the conclusion that this irritability was a 'condition of mental activity presenting some peculiar features': irritability, disorder of temper, and unreasonableness. His 'more accurate and extended observations' enabled him to link 'periods of unusual irritability with paroxysms of exacerbation' with 'retained urine salts, and especially to uric acid'. Fothergill found this conclusion to be perhaps 'more acceptable to charity than likely to be accepted by psychologists', although it would often be satisfactory and agreeable, he added, 'to explain anomalous and indefensible acts by this theory, and lay some of human frailty to the charge of uric acid'. He was, however, reluctant to relegate a more detailed description of his impressions even to a footnote:

but this excess of urine salts does seem to have a stimulant effect on the brain, and gouty people are usually possessed of some talent. The conclusions, so far, seem to indicate that many persons of good brains, but lacking in energy and inclination to think, are stimulated by retained uric acid into excellent thinking, and attain a reputation late in life. While in others, with small irritable 'foxy' brains, the disturbing effect of these retained excreta makes the cares of business, &c., quite intolerable. Retirement from business at first gives relief; but soon this irritability incites them to have something to do, and this too commonly is effected by becoming members of boards and committees, when this mental irritability takes the form of

mischievous perversity, of ill-controlled interference with everything and everybody. In this condition they remind the writer of nothing so much as a cancerous gland—no longer fulfilling any useful purpose, but merely a source of irritation to everything around them.

At the 8th International Medical Congress, held at Copenhagen in 1884, gout was not discussed as a topic as such, according to the Transactions, ¹⁰³ but Müller, ¹⁰⁴ in his paper On the Role of the Dyscrasies in the Etiology of the Neuroses and Psychoses, stated that he would not go into any details about gout and rheumatism and their connection with the nervous system, except to say that they were autogenic dyscrasies, i.e. manifestations of auto-intoxication of the body, and that they were awaiting further scientific explanation ('die nach weiterer wissenschaftlicher Aufklärung harren'). ¹⁰⁵

Lépine¹⁰⁶ spoke on intestinal auto-intoxication to the effect that 'dans beaucoup d'états morbides du tube digestif, avec stagnation des matières, il y a possibilité d'une auto-intoxication', and 'il me paraît incontestable que certaines urines renferment des principes toxiques organiques, et il est permis de supposer qu'ils ne sont pas sans influence sur les phénomènes morbides'.

Concluding this chapter, it should be mentioned that Rayner provided an excellent comprehensive overview of the topic under scrutiny, entitled Insanity From Gout (or 'cerebral disorder dependent on gouty toxaemia'), published in the Tuke's widely disseminated Dictionary of Psychological Medicine from 1892, 107 - today an indispensable source book and pathfinder to the history of psychiatry. Rayner emphasised that 'retrocession of gout is a well-recognised cause of apoplexy, but it may also result in mania, with or without epileptiform seizures, and in other mental disturbances'.

⁷¹ Mead R.: 'Medical precepts and cautions'. London: Brindley, 1751.

⁷² Perfect W.: 'Annals of Insanity. Comprising a Selection of curious and interesting Cases in the different Species of Lunacy, Melancholy, or Madness, with the Modes of practice in the Medical and Moral Treatment, as adopted in the Cure of each'. 5th Edn. London, s.a. [1809]. Case 52, pp.209–212: Arnold Press. cf. Berthier, op. cit., p.397 (Mathey A.: 'Nouvelles recherches sur les maladies de l'esprit'. 1816. Observation 31, p.335).

⁷³ Trotter T.: 'A view of the nervous temperament being a practical enquiry into the increasing prevalence, prevention, and treatment of those diseases commonly called nervous, bilious, stomach and liver complaints; indigestion; low spirits; gout, &c'. London, 1807. pp.226–228,304,309 (Reprint: New York: Arnold Press, 1976).

⁷⁴ Pinel P.: 'Traité médico-philosophique sur l'aliénation mentale'. 2nd Edn. Paris: Brosson, 1809. p.53. cf. Berthier, op. cit., p.389.

⁷⁵ Bayle ALJ.: 'Traité Des Maladies Du Cerveau Et de Ses Membranes'. Paris: Gabon, 1826, pp.416–117. (Reprint. New York: Arnold Press.) Other works by Bayle on gout, not sighted by this author, include 'Recherches sur l'Arachnitis chronique, la Gastrite et la Gastro-Entérite chroniques, et la Goutte, considérées comme causes de l'aliénation mentale'. Paris: Gabon, 1822, and 'Mémoire sur la Goutte anomale'. Brochure. Paris: Gabon, 1824.

⁷⁶ Esquirol E.: 'Des maladies mentales considérées sous les rapports médical, hygiénique et médico-légal'. Paris: Baillière, 1838. Vol.1, p.75. (Reprint. New York: Arnold Press.)

⁷⁷ Ouoted from Berthier, op. cit., p.393.

- ⁷⁸ Bufalini M.: 'Fondamenti Di Patologia Analitica. Prima Edizione Milanese. Esequitor sopra quella di Pesaro del 1830'. Milano, 1833. pp.508–529: 'Delle variazioni di proporzione fra i diversi prodotti dell'assimilazione organica'. ibid., Atassitrofia (Cl. II. Ord. V). p.742.
- ⁷⁹ Ellis WC.: 'A treatise on the nature, symptoms, causes, and treatment of insanity'. London: Holdsworth, 1838. pp.100–101. (Reprint. New York: Arnold Press.)
- 80 Morel B.A.: 'Traité des maladies mentales'. Paris, 1860. pp.148–150.
- ⁸¹ Gilbrin AA.: 'De la Diathèse Urique'. Thése. Paris, 1858. Quoted in Johnson, 1984, op. cit., ref.1, p.142. ref. 2, pp.202–203.
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