

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 1 Gout, uric acid, uric acid diathesis & mood disorders**

Lithium entered medicine in the mid-1850s as a remedy with which to treat gouty conditions where an excess of uric acid in the body was believed to be the underlying condition.

The history of medicine since the seventeenth century is replete with accounts of an assumed connection between gout and various mental diseases, predominantly mood disorders, and their accompanying treatment. The history of lithium treatment cannot be told without acknowledging and rendering these beliefs, no matter how erroneous they turned out to be.

Gout, a term derived from the Latin, *gutta*, to denote ‘the dropping’ of a morbid material from the blood in and around the joints is one of the oldest diseases described in medical literature.<sup>48</sup>

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<sup>48</sup> A comprehensive overview of the history of gout, its many forms and treatments (‘pre-lithium’), and rich bibliography is found in Copland J: ‘A dictionary of practical medicine’. Longman: London, 1844. Vol. II:33–61. cf. B. London’s invaluable comprehensive international bibliography: ‘Literature On Gout’, in *Practitioner* 1903;Aug.:337–353. Garrod AB: ‘The nature and treatment of gout and rheumatic gout’. Walton & Maberly: London, 1859 (and subsequent editions, in 1863 and 1876). Rodnan GP, Benedek TG: ‘Ancient therapeutic arts in the gout’. *Arthritis and Rheumatism* 1963;6:317–340. Atsmon A, De Vries A, Frank M: ‘Uric acid lithiasis’. Elsevier: Amsterdam, 1963. Copeman WS: ‘A short history of the gout and the rheumatic diseases’. University of California Press: Berkeley University of California Press, 1964. Talbott JH: ‘Gout’. 2nd Edn. Grune & Stratton: New York, 1964. Celsus on Medicine. Books I–IV. Harvard University Press, 1935. pp.463–465.

Uric acid was discovered in urinary calculi by Scheele<sup>49</sup> and Bergmann simultaneously in 1775,<sup>50</sup> and thence it became associated with gout. Wollaston<sup>51</sup> in 1797, and Pearson,<sup>52</sup> two years later, demonstrated its presence in gouty concretions.

In 1805 Parkinson advanced the important concept of uric acid diathesis.<sup>53</sup> He postulated that a tendency to periodical excess of uric acid in the blood might cause urinary gravel, uratic arthritis, rheumatic arthritis, rheumatism and gout. However, Scudamore, who divided gout into acute, chronic, and retrocedent gout,<sup>54</sup> cautioned that 'no very limited theory, and no one particular hypothesis, can be found applicable to explain the whole nature of gout'.<sup>55</sup> In 1847 Alfred Baring Garrod espoused the view that the blood of gouty patients contained an excess of uric acid, in the form of the urate of soda, thus apparently confirming the hypothesis.<sup>56</sup> This held sway until some time into the first decades of the twentieth century when it was finally abandoned as erroneous.

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<sup>49</sup> Scheele KW: 'Undersökning om blasestenen'. Kongl. Vetenskaps-Acad. Handl. 1776;37:327–332. (English translation in his 'Chemical Essays'. London 1786). Scheele KW: 'Opuscula', Leipzig, 1776;II:73. Johnson FN.: 'History of lithium therapy'. 1984, op. cit., p.140 (note 23). Scheele originally used the term 'lithic acid'.

<sup>50</sup> Atsmon A, et al.: 1963, op. cit.

<sup>51</sup> Wollaston WH: 'On gouty and urinary concretions'. Phil. Trans. (London) 1797;87:386–400, quoted in Johnson, 1984, op. cit.; cf. Jacobæus H: 'Indledning til en Diskussion om Urinsyre-Diatesens Væsen og Behandling'. [Dan.]. Ugeskr. Læg. 1906;5R;13:457–471. Faber E: 'Urinsyrediathesen'. [Dan.]. Ugeskr. Læg. 1911;73:751–771. Atsmon, 1963, op. cit.

<sup>52</sup> Pearson GH: Phil. Trans. London, 1798;87:15. Atsmon, 1963, op. cit.

<sup>53</sup> Parkinson J.: 'Observations on the nature and cure of gout; on the nodes of the joints; and on the influence of certain articles of diet, in gout, rheumatism, and gravel'. London: Symonds, 1805. Quoted here from Amdisen A.: 'The history of lithium'. Biol. Psychiatr. 1987;22:522-524. Amdisen A.: 'The first lithium era', in Johnson FN. (ed.): 'Depression & Mania. Modern lithium therapy'. Oxford: IRL Press, 1987. pp.24–28.

<sup>54</sup> cf. Garrod AB.: 'The nature and treatment of gout and rheumatic gout'. 1859, op. cit.

<sup>55</sup> Scudamore C.: 'A treatise on the nature and cure of gout'. London 1816, quoted here from Rasch C.: 'Om Forholdet mellem Hudsygdomme og den arthritiske diatese'. Hospitalstid. (Cph.) 1896;4R;4(48):1154. In 1884 H. Rendu intriguingly wrote that 'Aussi l'examen des diverses doctrines émises au sujet de la nature de la goutte est-il singulièrement stérile, car c'est l'énumération des erreurs du passé' (Dechambre's Dictionnaire 1884. vol. 10. pp.6–254. Quoted here from Strandgaard NJ.: 'Gigt og Urinsur Diatese'. Copenhagen: Lund, 1899:116–117).

<sup>56</sup> Garrod AB.: 'Observations on certain pathological conditions of the blood and urine in gout, rheumatism and Bright's disease'. Trans. Med. Chir. Soc. (Edinb.) 1848;31:83, cited by several authors. Copeman WS, 1964, op. cit.

Fernel considered the brain or rather the pericranium to be the primary source of gout.<sup>57</sup> Several other classic authors, the likes of Willis, Stahl, Boerhaave, Cullen, Leroy and Pinel taught that, as Cullen put it, gout was ‘manifestly an affection of the nervous system’.<sup>58</sup>

Very fittingly, in 1753 Liger compared gout, this *domina morborum*, to ‘Pandora’s box’.<sup>59</sup> However, it had become well differentiated from other forms of arthritis in 1683 when Sydenham, ‘the victim and historian of gout’ in his *Tractatus de podagra et hydrope* gave the classic description of gout, distinguishing between regular true or typical, and irregular or atypical gout.<sup>60</sup> ‘Melancholia, so called, is pre-eminently the inseparable companion of gout’, he taught.<sup>61</sup> ‘The mind suffers with the body, and which suffers most it is hard to say. So much do the mind and reason lose energy as energy is lost by the body - so susceptible and vacillating is the temper - such a trouble is the patient to others as well as to himself - that a fit of gout is a fit of bad temper’.<sup>62</sup> Stahl advocated the ‘neurotic’ theory of gout, and Cullen adopted his views.<sup>63</sup>

It was believed that irregular or abarticular gout often affected persons, who had never suffered from gout in the joints. If patients developed irregular gout, the gouty substance was to be driven back into the joints by all means. Thus, in his aphorism no. 1273 Boerhaave asserted that ‘Nothing can be more hurtful than to hinder the gouty matter [...] which cannot safely by any other way be carried off or corrected to discharge itself at the usual places [...] For if the retained matter seizes the brain, it occasions apoplexies, palsies, deliriums, debilities, tremors, lethargies, and universal

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<sup>57</sup> Quoted here from Berthier P.: ‘De la folie goutteuse’. *Ann. Méd.-Psychol.* 1869;1:389.

<sup>58</sup> loc. cit. Duckworth D.: ‘A plea for the neurotic theory of gout’. *Brain* 1880;3:1–22 (2). Duckworth refers to: ‘First lines of the practice physic’. Edited by John Thomson. Edinburgh, 1827. (vol. ii. Part i. chapt. xiv).

<sup>59</sup> Liger CL.: ‘Traité de la goutte’. 1753, p.318, cited here from Berthier, op. cit., p.392.

<sup>60</sup> Sydenham T.: ‘Tractatus de podagra et hydrope’. Londini: Kettilby, 1683. In English translation in his Works, published by the Sydenham Society, 1850;2:123-184, cited by many authors.

<sup>61</sup> cf. Roose R.: ‘Gout, and its relations to diseases of the liver and kidneys’. 5th Edn. London: Lewis, 1888. 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). Rayner H.: ‘Diathesis (insane)’, in ‘A dictionary of psychological medicine’. Edited by D. Hack Tuke. London: Churchill, 1892. Vol 1, pp.382–384.

<sup>62</sup> cf. Clouston TS.: ‘Clinical lectures on mental diseases’. 2nd Edn. London: Churchill, 1887. pp.463–465; 6th Edn. 1904, pp.506–507.

<sup>63</sup> cf. Roose R.: ‘Gout, and its relations to diseases of the liver and kidneys’. 5th Edn. London: Lewis, 1888, p.51. Luff AP.: ‘Gout. Its pathology and treatment’. London, Paris, New York & Melbourne, 1898, p.21.

convulsions',<sup>64</sup> thus the proverbial expression: *erumpente podagra, solvitur melancholia*.<sup>65</sup>

Musgrave in 1707 described *melancholia arthritica*,<sup>66</sup> and in 1763 the great nosologist, Boissier de Sauvages described *goutte mélancolique* in 'class VII, order I, chapt. I'.<sup>67</sup>

The view that mania could also be a manifestation of gout was put forward by Whytt<sup>68</sup> in 1765; it was in 1789 that Lorry<sup>69</sup> reported that the two conditions, melancholy and mania, could be caused by gout:—*la goutte se fixe au cerveau, pour déterminer le délire, ou plutôt la mélancolie et la manie*.

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<sup>64</sup> Rodnan and Benedek, *op. cit.*, 1963.

<sup>65</sup> Berthier, *op. cit.*

<sup>66</sup> Musgrave W.: 'De arthritide anomala'. Oxford, 1707. (1715, 1736), quoted here from Rasch C.: 'Om Forholdet mellem Hudsygdomme og den arthritiske diatese'. *Hospitalstid.* 1896;4R;4(48):1155.

<sup>67</sup> Berthier, *op. cit.*

<sup>68</sup> Whytt R.: 'Observations on the nature, causes, and cure of those disorders which have been commonly called nervous hypochondriac, or hysteric, to which are prefixed some remarks on the sympathy of the nerves'. Edinburgh: Balfour, 1765. p.166, quoted here from Berthier, *op. cit.*, p.392.

<sup>69</sup> Lorry AL.: 'De præcipuis morborum conversionibus'. Paris, 1789. p.280, cited here from Berthier, *ibid.*, p.393.