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**Asclepiades of Bithynia's Medical Molecular Theory and his
Contribution to Evolving Understandings of Mental Illness**

A thesis submitted to
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for the degree of
Doctor in Medicine

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Declaration

I declare that this thesis has not been submitted as an exercise for a degree at this or any other university and it is entirely my own work.

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Signed:

A handwritten signature in cursive script, appearing to read 'Frank Brady', written in dark ink.

Mr Frank Brady

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Dedication

This thesis is dedicated to my late dear wife Colette and to my four children and eleven grandchildren.

Abstract

Asclepiades of Bithynia (124 BC-40 BC) was a Greek physician who practiced and taught Greek medicine in Rome in the late second and early first century BC. His unique medical system was strongly influenced by Epicurean philosophy. He sought to construct a new theory of human disease derived in part from the atomic theory of chance and evolution described earlier by Democritus and Epicurus. He is generally accepted by most scholars as being the first leading representative of Greek theoretical medicine to work as a practicing physician in Rome. When he first arrived in Rome his knowledge of medicine and philosophy, coupled with his considerable rhetorical skills and personality allowed him not only to flourish as a physician, but to be accepted into the intellectual and sophisticated aristocratic circles that existed in Rome during the late Republican period. Asclepiades was boldly challenging the long-standing Hippocratic doctrine of the four bodily humors, as well as its benevolent nature axiom. Asclepiades held that a fully-fledged theory of matter was necessary for the understanding and practice of medicine and was positing an innovative systematic medical theory that drew extensively on Epicurean atomism. He was saying that the human body, as well as everything else in the universe, was composed of tiny, imperceptible particles, which he called onkoi. According to his theory these seamless masses were in perpetual motion, bouncing around forever within a void space, without having any providential intelligence at work in the universe to guide them. He postulated that these onkoi were of different shapes and sizes, lacking colour and sensitivity and possessing the capacity to aggregate together by chance to form larger masses that would ultimately form all of the components of the universe, including the human body. Unlike the indivisible theoretical atoms of Epicurus, Asclepiades was saying that these onkoi were uniquely capable of splitting into innumerable smaller fragments which would move around constantly within the void space. His mechanistic theory of medicine was saying that good health is maintained by the free and balanced motion of the onkoi through these pores and channels that lay within the void space, whereas disease is primarily the consequence of the blockage or impaction of the onkoi passing through the pores that are situated at particular sites throughout the human

body, with specific diseases resulting from such blockages at these different sites. This specific localization of pathological phenomena was fundamental to Asclepiades' approach to diagnosis and treatment. His approach to the management of disease, especially mental illnesses, was reasoned, humane and was in so many ways ahead of its time. As a result of his many contributions and his overall approach to patient care, this somewhat neglected physician is now considered by many medical historians as being the father of molecular medicine (Yapjakis, 2009). Asclepiades' ideas about the composition of the human body and disease processes at the microscopic level anticipated later developments in the scientific field, including the modern understanding of molecular biology and medicine.

This thesis explores the life and times of Asclepiades and how his unique theoretical framework for the understanding of human disease, which diverged from the dominant medical paradigms of his time, contributed to the promotion of a more humane approach to patient care, particularly in the context of mental health.

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Brady FA, Kelly BD. Asclepiades of Bithynia: Greek physician and medical reformer. *Irish Journal of Medical Science* 2023; 192 (4): 1775-1778.

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Chapter 1: Introduction

This chapter in the thesis provides a brief introductory background to Asclepiades of Bithynia (Section 1.1) and outlines the aims of this thesis (Section 1.2).

1.1 Background

Asclepiades of Bithynia (124 BC-40 BC) was a Greek physician who practiced and taught Greek medicine in Rome (Raynaud, 1862; Wellman, 1908 and 1929; Rawson, 1982; Polito, 1999; Yapijakis, 2009; Leith, 2012; Flemming, 2012; Brady and Kelly, 2023). He was born in 124 BC in Prusias-on-Sea in Bithynia which was then a Roman province on the north-western region of present-day Turkey. The eminent historian Elizabeth Rawson had said of him “that there was no intellectual figure at work in Rome in the period of the late Republic who had more originality and influence than the Bithynian doctor Asclepiades” (Rawson, 1982).

Among his many contributions, Asclepiades challenged the long-standing Hippocratic doctrine of the four humors. Influenced by Epicurean philosophy he sought to construct a new theory of human disease derived in part from the atomic theories of chance and evolution which had been earlier described by Democritus (c460 BC-c370 BC) and Epicurus (341 BC-270 BC). Against this background, Asclepiades’ practical approach to the management of physical and mental illnesses was both reasoned and humane, and a forerunner of later developments in psychiatry. Asclepiades is now considered by many scholars to be a pioneer of modern physical therapy, and the progenitor of a more humane approach to mental illness. Yapijakis accurately describes Asclepiades as “the father of molecular medicine” (Yapijakis, 2009 and 2018).

Recent decades have seen increased interest in Asclepiades and his work, especially his prescient contributions to clinical medicine, many of which predated modern approaches by several centuries (Brady and Kelly 2023). There is however, considerable academic work and research still to be done on this complex figure. This task is rendered difficult by the fact that none of Asclepiades’ writings remain, except for some fragments (Cocchi, 1758; Gumpert, 1794; Green, 1955). As a result,

Asclepiades is arguably best known through the testimony of other, often less sympathetic ancient writers, such as Pliny the Elder (23 AD–79 AD) and Galen (129 AD–216 AD). Even so, Asclepiades is generally acknowledged by most scholars as being the physician to have firmly established Greek medicine in Rome (Yapijakis, 2009; Leith, 2020) and merits continued attention as such.

Against this background, this thesis uses relevant sources to outline the background to Asclepiades' life and work, explore his contributions to medical thought and practice, and in particular to examine his contribution to evolving understandings of what is now known as mental illness. Particular attention is paid to the context in which Asclepiades lived and worked, and how his views were received at the time. To conclude, relevant conclusions are drawn and useful directions for future research and scholarship are suggested in order to shed further light on this pivotal, fascinating figure in the history of medicine.

1.2 Aims of this Thesis

This thesis aims to use primary sources (as much as feasible) and secondary sources to achieve the following aims:

- (a) *To provide a focused background to Asclepiades of Bithynia*, looking at medicine before Asclepiades' times (Section 3.1) the philosophical history of the Greek theory of matter (Section 3.2), medical practice in ancient Rome (Section 3.3), and what is known about the life and death of Asclepiades himself (Section 3.4);
- (b) *To outline and examine Asclepiades' thought and work, and the context within which he developed and implemented his theories*, especially his ideas in relation to “molecules”, “pores”, and “voids”, including parallels between his medical theory of molecules (*meree* or *corpuscula*) which are made of atom-like particles (*anarmoi oncoi*) and void spaces (pores or *poroi*) on the one hand, and on the other hand molecular medicine and molecular stereo-pathology (Section 4.1);

- (c) *To outline and examine Asclepiades' approach to treatment*, based on Asclepiades' view that "nature does not look after living organisms", which led him to propose the division of diseases into acute and chronic, and to suggest that patients with acute diseases should be treated swiftly, safely and pleasantly, and patients with incurable chronic diseases should be comforted (using treatments such as hydrotherapy, gentle massage, physical exercise, appropriate music, etc.); parallels with modern medicine are explored (Section 4.2);
- (d) *To outline and examine Asclepiades' ideas about mental illness and its management* and examine the ways in which Asclepiades' humane approach contrasted with the other treatments at that time and anticipated future developments in the field of psychiatry and mental health care (Section 4.3). Special attention is given to the role that Asclepiades' own school played in the later formation of the Methodic School (Section 4.4.4).
- (e) *To explore the relevance of the schools (sects) of medicine of Asclepiades' time*, including the Dogmatic School, also known as the Rational or Logical School, which had a teaching philosophy emphasising theoretical principles (4.4.1) as well as the Empirical School which was founded in the middle or towards the end of the third century BC, which found its philosophical roots in skepticism (4.4.2). The significant role that Asclepiades made in providing the foundations for the subsequent Methodic School (4.4.3). Lastly, the somewhat under reported contribution that Asclepiades' own Medical School (4.4.4) made in securing the installation of Greek medicine in Rome and the surrounding mediterranean area is explored.
- (f) *To examine the views of Asclepiades' supporters and detractors*, including the nature of their opinions and beliefs about medicine, and how their views differed from those of Asclepiades (Section 4.5); and
- (g) *To present relevant overall conclusions* (Section 5.1) and *outline useful directions for future research* about Asclepiades, his work, and his life and times (Section 5.2).

Chapter 2: Methods

The methods of medical history research differ from research methodologies in other areas of medicine (Burnham, 2005). Systematic literature searches, common in other areas of medical research, are often insufficient for the medical historical literature. While systematic searches are helpful in identifying a certain portion of the recent academic literature, they need to be supplemented by the interrogation of other historical sources, standard translations of works, and where available, ancient texts. This multi-model approach is especially necessary in the case of Asclepiades. With that in mind this Chapter of the thesis outlines the methods used to identify and explore the writings of Asclepiades of Bithynia (Section 2.1) and available ancient texts and secondary literature relating to Asclepiades (Section 2.2).

2.1 The Writings of Asclepiades of Bithynia

Historically, Asclepiades of Bithynia stood at a crucial point in the development of Greek medicine, and, in the words of Rawson, “there was no intellectual figure at work in Rome in the period of the late Republic who had more originality and influence than the Bithynian doctor Asclepiades” (Rawson, 1982).

Despite his significance, Asclepiades remains a relatively obscure and somewhat shadowy figure in ancient medical history. None of his writings have survived apart from some fragments of his works in the works of other authorities. As a result, ancient testimony relating to Asclepiades comes from some forty different authors (Cocchi, 1758). In consequence, it is necessary to rely on the testimony of these later and often hostile writers, whose views on Asclepiades are frequently inconsistent and often opinionated. This is especially true in the case of as Pliny the Elder (23 AD–79 AD) and later, Galen (129 AD-200 or 216 AD) (Brock, 2016). Against this background, this research is based on literature searches relevant to this thesis’ theme, consideration of

the secondary literature, and review of relevant fragments of Asclepiades' work that survive (Green, 1955; Thumiger and Singer, 2018).

For the literature searches, pertinent key words ("Asclepiades", "Ancient Graeco- Roman medicine) were used to search for papers in PubMed, Google Scholar, Brill, JSTOR, and the Loeb Classical Library, as well as general Internet searches. Relevant materials were sourced, identified and assembled. Key ancient texts from this overview of the historical literature included *Discorso Primo Sopra Asclepiade* (Cocchi, 1758), *Asclepiadis Bithyniae Fragmenta* (1794), *On Acute and On Chronic Diseases* (Caelius Aurelianus; transl., Drabkin, 1950), *Naturalis Historia*, (Pliny the Elder, specifically, Book 26, Chapters 7 and 8), and *On the Natural Faculties* (Galen; 3 books on Medicine and Medical topics; transl Brock, 1916). These source materials are discussed further in this thesis.

Other ancient sources are not available in primary format and are discussed in this thesis based on secondary sources, as is customary in this literature. For example, it is generally believed that Hippocrates did not write many treatises himself, and most of the writings that are attributed to him were written by his many followers, and so this author discusses the work of Hippocrates' followers based on a standard version and translation of the Hippocratic Corpus, i.e., *Hippocrates: An English Translation* (Jones, 1923).

The perspectives presented in ancient texts are further explored and contextualized throughout this thesis, as the opinions and (arguably) biases of the various writers are relevant to the context of the theories outlined and the story of Asclepiades life and work.

2.2 Available Ancient Texts and Secondary Literature

Key texts which relate to Asclepiades' life and work, and used to inform this thesis, are, in summary:

- Antonio Cocchi: *Discorso Primo Sopra Asclepiade* (Florence, 1758).
- Christian Gottlieb Gumpert: *Asclepiadi Bithyni Fragmenta* (Weimer, 1794).

- Caelius Aurelianus: “On Acute Diseases and On Chronic Diseases” (the 5th Century AD). Edited and translated into English by I. E .Drabkin (1950).
- Pliny the Elder: *Naturalis Historia*; specifically, Book 26, chapters 7 and 8.
- Cornelius Celsus: *De Medicina*.
- Dioscorides: *De Materia Medica*.
- Scribonius Largus: *Compositiones Medicamentorum*.
- Apuleius: “Florida”.
- Galen: “On the Natural Faculties” (3 books on Medicine and Medical topics). translated into English by Arthur John Brock in 1916 for the Loeb Classical Library.

In order to contextualise later chapters in this thesis, it is necessary to provide further information about some of these authors.

2.2.1 Antonio Cocchi: *Discorso Primo Sopra Asclepiade (Florence), 1758*

Antonio Cocchi was an Italian physician, naturalist and writer. He was born in 1695 in Benevento, Italy. He held the chair of Anatomy at the Royal Hospital of Santa Maria Nuova in Florence, Italy. His writing style was characterised by purity of diction and Rawson has said that he was regarded in his own time as a model for scientific writing (Rawson, 1982). He lived in England for three years and was acquainted with Sir Isaac Newton (1643- 1727). He was elected a Fellow of the Royal Society.

In 1759, Cocchi wrote a book on the Life and Writings of Asclepiades titled: *Discorso Primo Sopra Asclepiade*, which appeared anonymously as an English translation in 1762. This English translation of Cocchi’s work was most likely from a previous Italian edition. However, it was of relatively poor quality. In the early 1950’s, Dr Sidney Licht of New Haven, Connecticut, USA asked Dr Montraville Green, Professor of Anatomy at Harvard University, to produce a new and improved English translation of a Cocchi reprint which had been published in Milan in 1824. Green’s subsequent English translation of the Cocchi reprint was published in 1955 by Elizabeth Licht of Waverly Press, Baltimore USA (Green, 1955).

Cocchi was undoubtedly an admirer and strong supporter of Asclepiades and Epicurus “who, even if he did not really liberate Greece from stupidity, as the poet Menander sings of him, at least revived the taste for natural science, restoring to light some of the opinions of the old physicists, especially of Anaxagoras and Democritus and bringing men back to the search for the mechanical causes of the perceptible appearances of things, from the consideration of which they had somewhat removed by the three other most celebrated schools, Platonic, Peripatetic, and Stoic” (Cocchi, 1758; Green, 1955). Cocchi’s *Discorso Primo Sopra Asclepiade* still contains an amount of very useful information on the life and times of Asclepiades, which remains relevant. However, much of what Cocchi said in relation to Asclepiades’ early education in Bithynia and possibly in related areas (such as in the Kingdoms of Mysia and Phrygia) is considered by many scholars to be highly speculative. Raynaud had pointed out that Cocchi was most likely endeavouring to embellish the virtues of Asclepiades (Raynaud, 1862). More recently, Rawson said that Cocchi’s *Discorso Primo Sopra Asclepiade* “while learned and often penetrating, is over-enthusiastic about his subjects’ moral virtues” (Rawson, 1982; p.361[22]).

This thesis uses a copy of Montraville Green’s 1955 book which not only contains Cocchi’s *Discorso Primo Sopra Asclepiade* but also Fragments of Asclepiades of Bithynia which was arranged and edited by Christian Gottlieb Gumpert (Gumpert, 1794).

2.2.2 Christian Gottlieb Gumpert: *Asclepiadi Bithyni Fragmenta* (1794)

Christian Gottlieb Gumpert (1772-1832) was a Polish physician and medical historian. While he was studying at the University of Weimer in Germany, he collected all of the fragments of the writings of Asclepiades that were available at the time and published these as a book in 1794: *Asclepiadi Bithyni Fragmenta*. While most of Gumpert’s work was in Greek and Latin, some portions of his text were in French, German, and Italian (Gumpert, 1794). Nineteen of Asclepiades’ “Titles of Work”, with text references, were sourced mainly from Montraville Green’s book (1955; chapter III, pp. 66-82):

- a) “Alopecia” (Galen:de compositione medicamentorum pergenera XII.410K);
- b) “On Respiration and the Pulses” (Galen.de differ.puls. IV.p.61.T.III);
- c) “On Enemas” (Cael.Aurel.de morbis chronicis II.184);
- d) “On Ulcers” (Cassius Quaest.med.probl. XXXX);
- e) “On Periodic Fevers” (Cael.Aurel.de morbis acutis. II,56);
- f) “Definitions” (Cael.Aurel.de morbis acutis II.89);
- g) “About the More Obscure Books of Hippocrates” (Galen. Comment.I.in Hippocr.de offic.med.T.V.P.665);
- h) “The Duties of Doctors” (Galen.Comment.I.in Hippocr.de office.med. T.V.P.667,674);
- i) “Aphorisms of Hippocrates” (Cael. Aurel.de morbis acutis II.158);
- j) “Books against Erasistratus about Preparations” (Cael. Aurel.I.acut.p.2.lib.I.IV);
- k) “Three Books about Rapid or Acute Diseases” (Cael. Aurel.lib.II.acute.C.39. p.176);
- l) “About Pulses” (Galen.T.III.p.51.de differ.puls.lib.IV);
- m) “Books to Geminus on Hygiene” (Cael. Aurel.chron.C.7.p.386);
- n) “Volumes for Mithridates of Precepts sent from Rome” (Pliny. H.N.XXV.3);
- o) “Safeguarding the Health” (Cels.1,3,p.29; Cael.Aurel.de morbis acutis I.112);
- p) “About Elements” (Galen.de elementis secundum Hippocratem I.487K);
- q) “The Administration of Wine” (Sext.Empiric.adv.Logic. I,f.91.p.338; Pliny, N.H. XXX.31-32; Cael. Aurel. De morbis acutis II.158);
- r) “On Dropsy” (Cael. Aurel. De morbis chronicis, III.122);
- s) “On Wounds” (Cassus Iatrosophista, Problemata 40).
- t) “Concerning Cardiac Lues”(Cael.Aurel.lib.II.acute.C.p.176).

2.2.3 Caelius Aurelianus: “On Acute Diseases and on Chronic Diseases”

In 1950, Drabkin produced an excellent English translation of Caelius Aurelianus' Latin version of Soranus' original major work (Drabkin, 1950). Drabkin's English translation has come to be recognised as a monument of classical scholarship.

Caelius was a Roman citizen physician from Sicca, an ancient Roman town in the ancient kingdom of Numidia in Northwest Africa (in modern-day Tunisia). His date of birth is not known. However, based on linguistic and stylistic comparison with other ancient writers of the time, most scholars feel that Caelius most likely lived in the sixth century AD (Drabkin, 1950). He was a follower of the Methodic School of Medicine. His writings contain the clearest and most accurate diagnoses found amongst many of the ancient medical writers. He is best known for his fifth century translation from the Greek into Latin of Soranus' magnum opus, "On Acute Diseases and On Chronic Diseases". Soranus wrote his work in the first century AD, and it contained most of Asclepiades' theory of medicine and his methods of treatment.

This thesis uses a copy of Drabkin's 1950 book, which contains multiple and detailed references in English to Asclepiades' theories and on his medical practices.

2.2.4 *Pliny the Elder: Naturalis Historia*

Gaius Plinius Secundus (Pliny the Elder) was born in either 23 AD or 24 AD into a wealthy aristocratic equestrian family which had strong political connections in Rome. He was considered to have been an eccentric workaholic who never married or had any children. At the age of 23 years, he began a military career in the Roman army while at the same time studying law. In 47 AD he went as a cadet with the Roman army to fight in Germany. On his return from Germany, he took up residence on the Equiline Hill in Rome, where, tiring of practicing law, he devoted most of his time to writing on many diverse topics, a practice that he started whilst on active army service in Germany.

Pliny was a prodigious author who combined his scholarly writing activities with a busy career as an imperial administrator (procurator) for emperor Vespasian. From a medical perspective, Pliny's most famous production was his monumental Natural History (*Naturalis Historia*), which was divided into 37 books, organized into 10

volumes. This immense undertaking, which still survives, encompassed a wide variety of topics relating to the natural world (Rackham, Jones, Eichholz, 1938). While not a physician himself, 12 of Pliny's books (20-32) deal exclusively with medicine and medical topics (Bostok, 1857; Reynolds, 1986; Nutton, 1986; Wallace-Hadrill, 1990; Healy, 1999; Yapijakis, 2009; Leith, 2019). In book 26 of his *Naturalis Historia*, Pliny has provided most of our knowledge on Asclepiades, albeit much of it written in a very biased and frequently sarcastic manner. Like Cato before him, Pliny had a personal bitterness and irreconcilable hostility towards all things Greek, especially Greek physicians. This undoubtedly explains his vindictive and distorted image of Asclepiades (Benedum, 1967; Rawson, 1982; Yapijakis, 2009; Leith, 2019).

Pliny's entire *Naturalis Historia* was translated into English in 1938 by Rackham, Jones and Eichholz for the Loeb Classical Library (Rackham, Jones, Eichholz, 1938). This important library was founded in 1911 by James Loeb and is published free and distributed by Harvard University Press. Pliny's contentious views on Asclepiades are in Book 26 of *Naturalis Historia* in Chapters 7 ("The New System of Medicine: Asclepiades the physician") and 8 ("The Changes Effected by Asclepiades in the Practice of Medicine").

This thesis uses a full copy of the Loeb Classical Library's translation into English of Pliny's *Naturalis Historia* that had been undertaken by Rackham and his colleagues to analyze and assess Pliny's polemic views on Asclepiades, as outlined by him in Chapters 7 and 8 of Book 26 (Rackham, Jones, Eichholz, 1938).

2.2.5 Aulus Cornelius Celsus: *De Medicina*

Aulus Cornelius Celsus (25 BC-50 AD) was a distinguished Roman encyclopaedist. It is unclear whether Celsus was a physician; this is still the subject of scholarly debate (Greive, 1756; Spencer, 1926; Köckerling et al., 2013). In the early first century AD, Celsus composed an eight-volume compendium on medical matters, including two books on surgery. His treatise on medicine was titled *De Medicina*. It is the only surviving section of a much larger encyclopaedia. *De Medicina* draws upon knowledge

from ancient Greek works and covers the topics of known diseases of the time and the therapeutic methods used in an attempt to cure them (Donaldson, 2014).

De Medicina was originally written in Latin and has been considered by many scholars to have been the first and probably the best book in medicine of that time (Green, 1955). In 1478, in the city of Florence, this became the first complete textbook of medicine to be published after the introduction of the printing press (Donaldson, 2014). There are, however, some scholars who have cast doubts as to whether Celsus was in fact the author of *De Medicina* or whether he was just a general editor and compiler of the larger encyclopaedia (Talamonti et al, 2020). Because he was a Roman, it is most surprising that Pliny does not mention Celsus or take any account of his medical encyclopaedia, simply saying that “very few Romans had (ever) touched such a subject (i.e. medicine)” (Pliny, H.N. XXIX, capl., pp. 5,8, 669).

Celsus spoke favourably of Asclepiades in *De Medicina*, writing that “by his concentration on the healthy regime (i.e. dietetics), as opposed to pharmacology (drugs, herbs), or surgery, he [Asclepiades] had introduced an entirely new epoch” (Celsus proem. II). Celsus also mentions that “he held Asclepiades in high esteem” and referred to him as “a good author of many things which he himself had achieved”, adding that “he [Celsus] valued himself as being a follower of Asclepiades”. This thesis uses an English-language copy of *De Medicina* from the Loeb Classical Library to explore what Celsus said about Asclepiades, notwithstanding the unresolved matter of whether Celsus was the sole author or editor of *De Medicina* (Donaldson, 2014).

2.2.6 *Pedanius Dioscorides: De Materia Medica*

Pedanius Dioscorides (c40 AD-90 AD) was a Greek physician, pharmacologist and botanist. The name Pedanius is Roman, and this would seem to suggest that Dioscorides most likely was sponsored by a Roman aristocrat to become a Roman citizen. He was employed by the Roman army and travelled widely with them to Greece, Crete, Egypt, and Petra. In around 65 AD, after much personal direct observation of plants and having had practical experience with the medicinal use of herbs, Dioscorides wrote his monumental work which he called *De Materia Medica*.

This is a five-volume book concentrating on the preparation, properties, and testing of hundreds of drugs and herbs.

Dioscorides' encyclopaedia of herbal medicine and related medicinal substances was widely read for more than 1,500 years. As a result, *De Materia Medica* is the prime historical source of information about the various medicines and herbs that were used by the Greeks and Romans as well as other cultures of antiquity. The work presents details on about 600 different plants and formed the core of the European pharmacopeia up to the nineteenth century. Dioscorides was a supporter of Asclepiades. He wrote in his *De Materia Medica* that many of his major drug sources were Asclepiadean (Norton, 2006).

2.2.7 Scribonius Largus: *Compositiones Medicamentorum*

Not much is known about the early life of Scribonius. He was born circa 1 AD, most likely in Sicily, and died in circa 50 AD (Hamilton, 1986). He became the pharmacologist and court physician to the emperor Claudius. In 47 AD, at the request of Caius Julius Callistus, an imperial official and the emperor's freedman, Scribonius drew up a comprehensive list of medical prescriptions that formed the basis of his monumental *Compositiones Medicamentorum*, which was set out in 271 separate chapters. Scribonius was one of the first authors to write about medicine in the Latin language. As a Roman army doctor, he accompanied Claudius on the emperor's campaign to Britain. It is believed that he wrote most of *Compositiones Medicamentorum* while he was abroad, probably during the period 43 AD-47 AD (Cambiaghi and Sconocchia, 2018).

Scribonius Largus bestows the highest praise on Asclepiades by mentioning "Asclepiades' pills...the best preparation for artery trouble". He goes on to call Asclepiades "*Asclepiades, maximus, actor, medineae*" ("Asclepiades medicine's greatest authorities") (Scrib. Larg. Comp.pref.7; Cocchi, 1758; Sconocchia, 1983; Bernhold, 2011; Cambiaghi and Sconocchia, 2018).

However, in the fifth century much of Scribonius' work was appropriated by Marcellus Empiricus without any acknowledgement to the original author's work (Ross and Nutton, 2016).

This thesis uses a copy of *Compositiones Medicamentorum* from the Loeb Classical Library, in conjunction with Scarborough's published paper on "The drug lore of Asclepiades of Bithynia" (Scarborough, 1975), to discuss Asclepiades' judicious and careful use of drugs and medicinal herbs which he said should only be used in selected clinical situations. This will be explored to counter the views of scholars who have suggested that Asclepiades never advised drug therapy.

2.2.8 *Apuleius: The Apologia of Florida of Apuleius of Madura*

Apuleius was a Numidian Latin prose writer, philosopher, and rhetorician who was born in 124 AD in the Roman-Berber city of Madauros which is now a town called M'Daurouch situated in modern-day Algeria. Madauros was a former diocese of the Catholic Church and Saint Augustine of Hippo received part of his early education there (Harrison, 2004).

A collection of extracts of the speeches and lectures delivered by Apuleius in North Africa have survived as a compilation of 23 such extracts. A further five fragments were subsequently added. This collection of 28 extracts and fragments became known as *The Apologia of Florida of Apuleius of Madura*. The Florida was translated into English by H.E. Butler in 1909 (Lee, 2006).

Extract number 19 of the Florida is titled: "A story of the physician Asclepiades." In this extract Apuleius said of Asclepiades "that he ranks amongst the greatest of doctors, ...accepting that Hippocrates was the very greatest. Apuleius said that Asclepiades was the first to discover the use of wine as a remedy". Apuleius goes on to relate in great detail, how Asclepiades rescued a man, supposed to be dead, from on his own funeral bier. This thesis uses a copy of the "Florida of Apuleius" to discuss these themes in more detail.

2.2.9 *Galen: De Naturalibus Facultatibus*

Aelius Galenus or Claudius Galenus, often anglicized to Galen or Galen of Pergamon, was an illustrious Greek physician and philosopher, as well as being a prodigious writer. He was perpetually inquisitive, even in areas remote from medicine (such as logic and linguistics). He was an important logician who wrote major works on the so-called “scientific method” (Daremborg, 1853).

Galen was born on 129 AD during the reign of the emperor Hadrian in the famous cultural city of Pergamon situated in present-day Turkey. Pergamon was renowned for its temple to Asclepius and for its magnificent library. Galen is generally considered to be one of the most accomplished and influential medical researchers of antiquity. His views on medicine dominated and influenced Western medical science for more than 1,300 years up to the mid-seventeenth century in Europe, as well as having had a major influence in the Byzantine and Muslim Middle Eastern medical world.

Galen was the son of Aelius Nicon, a wealthy architect and builder, who had many eclectic interests and was schooled in mathematics, philosophy and logic. Galen received a comprehensive liberal education that his father believed would prepare him for a successful career in later life (Nutton, 2005; Potter and Mattingly, 2010).

Following on from his early education, and with no expense spared, Galen, at 16 years of age, began his medical studies in the famous Asclepieum in Pergamon under the best tutelage of the Greek physicians Aescnion, Stratonicus, and Satyrus. When his father died in 149 AD he left his son, at 19 years of age, an independent and very wealthy young man.

Galen was now able to travel widely, exposing himself to a wide variety of medical theories while visiting and studying in the great medical schools at Smyrna (Izmir), Corinth, and Crete before finally arriving at the renowned medical school in Alexandria, Egypt. In 157 AD, after about a decade of study, Galen returned to Pergamon where he served as surgeon to a troop of gladiators maintained by the high priest of Asia.

In 162 AD, the ambitious Galen moved to Rome. He quickly established a considerable reputation there by performing in public dissections and anatomical demonstrations on animals. His enormous medical knowledge, oratorical skills, wealthy

background, and social contacts greatly helped his growing reputation as both a physician and a philosopher and he was soon firmly established in the aristocratic intellectual life of Rome.

In 166 AD, Galen abruptly left Rome to return to Pergamon. He claimed that his leaving Rome at that time was prompted by what he considered to be the intolerable envy and jealousy of his colleagues. However, some scholars take the view that he was leaving Rome because of his knowledge of an impending plague that was to strike Rome at that time. In any case, his respite was short because in 168 AD he was called back to Rome by the joint emperors Lucius Verus and Marcus Aurelius to accompany them as chief physician to the Roman army, which was undertaking a military campaign in Northern Italy and Germany. During this campaign, Galen took time to continue to write extensively on medical matters. On his return to Rome, he subsequently served as chief physician to several later Roman Emperors.

Galen was one of the last great creative physicians of antiquity and probably died in Rome 200 AD, although Nutton has said that it may have been 10 years later (Nutton, 1973).

While Galen was a strong supporter of the Hippocratic four humoral approach to medicine, he modified the classic Hippocratic theory by arguing that the humoral imbalances responsible for disease could also be located in specific organs in the human body as well as to the body as a whole. This modification of the traditional Hippocratic method allowed Galenic physicians to make more precise diagnoses and to prescribe specific remedies to restore the body's balance of the humors.

Galen was a prodigious writer. His written output was so profuse that his surviving texts represent nearly half of all of the extant medical literature from ancient Greece. A fire in the Temple of Peace in 190 AD, where he had deposited many of his manuscripts for safe keeping, destroyed important parts of Galen's extensive collection (Kotric and Walters, 1979; Ustun, 2004). Even so, Galen's surviving medical writings encompass almost every aspect of medical theory and practice of his era. In addition to summarizing the state of medicine at the height of the Roman empire, he reports on his own important advances in anatomy, physiology and therapeutics. Notwithstanding his devotion to science, Galen could be both acrimonious and polemic (Prioreshi, 1998).

Galen's key extant works are to be found in his *Naturalibus Facultatibus*, which was a monumental undertaking in three books (Johnston, 2009).

Galen's work continued to be influential long after his death. Among many factors which tended to stimulate and awaken European minds in the mid-fifteenth century, was the re-discovery of the Greek classics which were being brought to Europe by scholars who had fled from Byzantium following the fall of Constantinople to the Turks in 1453. The Arabo-scholastic versions of Aristotle and Galen were, as a result, confronted by their Greek originals at this time. Prominent in this movement was the distinguished English physician Thomas Lynacre (1460-1524), whose many achievements included obtaining of a Royal Charter for the foundation of the Royal College of Physicians in London (which made him its first president).

During Lynacre's time in Italy, he gained an extraordinary zeal for the "New Learning" and on his return to England he devoted his time to making Galen accessible to the readers of Latin. The *De Naturalibus Facultatibus* appeared in London in 1523. In addition, Arthur John Brock translated Galen's three books from the original Latin into English, and this English version, "On the Natural Faculties", was deposited in the Loeb Classical Library (Brock, 1916).

As already mentioned, Galen was a staunch supporter of the Hippocratic humoral theory of medicine and treated with contempt, sarcasm, and ridicule the mechanistic atomic theories of Asclepiades and those of the subsequent Methodic School of Medicine (Horne, 1963). However, while he was contemptuous of the Methodist physician Thessalus, he did hold the Methodist physician Soranus of Ephesus in high regard (Drabkin, 1950).

This thesis uses Brock's 1916 translation of three books of Galen's "On the Natural Faculties". Most of Galen's polemic views on Asclepiades are contained in Book 1, but Asclepiades is also mentioned in Books 2 and 3. Galen is generally scathing, sarcastic, and dismissive of the theories and medical practices that Asclepiades promulgated. Galen also vigorously attacked all of the previous ancient physiological atomic theories, especially those that were posited by Erasistratus and Asclepiades (Brock, 1916).

Chapter 3: Background to Asclepiades of Bithynia

This chapter provides a background to the life and work of Asclepiades of Bithynia, examining medicine before Asclepiades' time (Section 3.1) and exploring what is known about the life and death of Asclepiades himself (Section 3.2).

3.1 Graeco-Roman Medicine before Asclepiades of Bithynia

3.1.1 *Early Greek Medicine*

There were many healing gods in Greek mythology, and the most famous one of antiquity was the Greek god Asclepius or Asklepios (in Latin he was called Asclepius or Aesculapius). He was believed to have been the son of Apollo and probably lived in the late thirteenth century BC. The Hippocratic Oath opens with "I swear by Apollo physician, by Asclepius, by Health, by Heal-all and by the gods and goddesses..." (Miles, 2004). In Greek mythology, Zeus killed Asclepius when hit by a thunderbolt. As recounted in Homer's "Iliad", Asclepius' sons, Machaon and Podalirius continued their father's work by serving in Agamemnon's army in the Trojan Wars (Platt, 1894). Hygeia and Panacea were the two daughters of Asclepius, Hygeia being the goddess of health and cleanliness, while Panacea was the goddess of universal healing.

Temples to Asclepius started to flourish all over the ancient Mediterranean, and well on into the Christian era. The most celebrated healing sanctuary in the classical world was established in the region of Epidaurus, a small city state on the Saronic Gulf in southern Greece and was dedicated to Asclepius.

People would come to these Healing Temples, which were known as Asclepieia in Greek and Aesculapians in Latin, in order to make offerings (donaria) to Asclepius in the hope of obtaining a cure or to give thanks for having received one. As part of this ritual worship, and to find out what was the right cure for their ailments, worshippers would spend a night in a large sleeping hall within the temple, known as the enkoimeteria and in their dreams the god himself would advise them as to what

they had to do to regain health. The temple priest would assist these worshippers in interpreting their dreams, with accompanying incantations, in a practice which was known as an “incubation”. When a temple to Asclepius was being built in a new location, it was necessary to first bring a cult object from the great sacred Temple in Epidaurus to the new temple site, in order to establish the presence of the healing god in the proposed new temple (King, 2006; Nutton, 2006). The Asclepieia, including that of Epidaurus, were always built near abundant fresh water supply and often near thermal springs, since sanitation, hygiene and several therapeutic procedures depended on a water source that was embedded in the sanctuary (Yannopoulos, et al. 2017; Angelakis, et al. 2020; Voudouris, et al. 2023).

According to legend, a plague hit Rome in 292 BC, leading the Roman Senate to build a new temple to Asclepius in Rome. After a priestly consultation with the augurs and with the ancient Sibylline Books, and having gained a favorable response, the Senate subsequently sent a delegation of Roman elders to the temple Epidaurus in order to obtain a cult object of the god Asclepius and bring it back to Rome so it could be placed in the new Roman Temple (Edelstein, 1967). Instead of obtaining a statue of the healing god which they had hoped for on their arrival in Epidaurus, the elders were given a sacred snake (serpent) instead. Legend has it that during the propitiatory rites, the snake slithered from the sanctuary and hid in one of the Roman ships.

Certain that this was a sign of the god’s favour the Roman delegation quickly returned to Rome. On arrival back in Rome the snake escaped from the ship, only to reappear on the Tiber Island thus marking the site where the Temple was to be built. Work began on constructing the temple. It was dedicated to Asclepius in 289 BC. Needless to say, the plague subsequently stopped with miraculous speed (Edelstein, 1967; Nutton, 2005). The snake (or serpent) soon became a lasting symbol of the wisdom of the medicine-man and of the Art of Medicine (King, 2006).

Asclepius is also credited by some scholars with being the first to apply music as a form of therapy in treating mental illnesses (Conrad, 2010; Kleisariis et al, 2014). The theme of music as therapy is explored further in this thesis in the context of Asclepiades.

Alcmaeon of Croton (540 BC-500 BC), a Greek physician-philosopher, was born in the Greek city of Croton in modern day southern Italy. He lived in the sixth century BC, but his precise date of birth and early life has not been agreed. What is known is that he was in Croton around the same time as Pythagoras was located there. He founded a medical school in Croton that the historian Herodotus said was the best of its kind in the Greek world (Debernardi et al, 2010). He appears to have incorporated many of the teachings of Pythagoras into his writings (Kahn, 2001; Riedweg, 2002). He is credited with being first to have introduced the concept that the human brain was the focal point of intelligence and consciousness (Kahn, 2001). He argued that the brain was the most important organ in the body, controlling all the body's functions. He postulated that the brain was the seat of all the senses and that different areas of the brain were responsible for detecting different sensory experiences such as sight, hearing, taste and smell, but curiously not the sense of touch. He also gave a description of the optic nerve and traced its path back to the brain. Alcmaeon asserted that a central nervous system was the physical source of mental activity, and that cerebral metabolism and stability of mental health was based on the proper balance of the "humoral fluxes." He was a pioneer in applying the metaphor of the "balance of the opposites" that constitutes the healthy human body. Interestingly, he postulated a concept of pores and channels which he felt connected to the senses within the brain (Solmen, 1961). Like other philosophers of his time, Alcmaeon thought about the natural life elements that contributed later to the Four Element Theory that was put forward by Empedocles (see below). Alcmaeon's ideas laid the foundation for later philosophical and scientific debates about the relationship between the body and the mind and his ideas continue to influence thinking about these issues to the present day (Kahn, 2001; Delenardi et al, 2010). The historian Herodotus said that Alcmaeon's medical school in Croton was, "the best in the Greek world" (Delernardi et al, 2010).

Diogenes Laertius (180 AD-240 AD), the principal biographer of Greek philosophy, mentioned that some had claimed that philosophy had been started by non-Greeks ("barbarians") Persian Magi, Babylonian Chaldeans, Egyptian Priests, Celtic Druids or even a mythical Phoenician, Mochus or Moschus ((Diogenes Laërtius; 1). While there is no written record of his life, oral tradition mentioned by the Platonist

Ofellius Laetus, the Stoic Posidonius and the Neoplatonist Iamblichus says that Mochus had a theory of matter based on logic, intuition, and religious revelation (Sedley, 1998). Diogenes dismisses as erroneous that claim and suggests that philosophy is a creation of Greek culture (Diogenes Laërtius; 1-15). Philosophy (“love of wisdom” in Greek) was radically different from religious myths of other nations since it attempted to use reason and empirical analogy in order to explain nature (Yapijakis, 2009).

In Greek antiquity, cosmogenic ideas originated in the eighth and seventh centuries BC. These ideas were essentially religious. Legendary descriptions of the origin of the world were a belief that there was a cosmic egg from which all things were said to have been produced at the beginning of our world (Pearce, 1973). These religious and magical beliefs had dominated human minds for millennia until philosophy started to flourish in the Greek world in about the sixth century BC. The Greek philosophers of that period were intellectual thinkers who were teaching themselves to solve problems by reason alone as in abstract reasoning detached from experimental learning. It is generally accepted that philosophy, as we understand it today, is a Greek creation (Farrington, 2000; Yapijakis, 2009).

A central intellectual effort of these Greek philosophers was their desire to reduce the vastness of the universe to its fundamental elements and to theorize that there was a single unit or elemental particle that composed all of the universe. In ancient Greek philosophy, the word *arche* (*arkhe*) was believed by these philosophers to be the “first principle”, or “first element” of everything that exists in our world. The concept of the *arche* is deeply linked to monism, the belief that says that all of the universe is derived from a single element or particle (Lee, 2017). Groups of pre-Socratic philosophers, which included Thales of Miletus (c624 BC- c548 BC), were starting a long tradition of attempts to try and explain nature by using experience that was based on the senses, as well as imagination which was based on empirical analysis and random thought (Farrington, 2000; Yapijakis, 2009).

3.1.2 *Thales of Miletus*

Thales was a famous Greek mathematician and astronomer. He was born in the ancient city of Miletus in circa 624 BC. Miletus was one of the great Ionian colonies situated on the eastern Aegean coast of Asia Minor close to the city of Belat in modern day Turkey. There has been some debate as to whether he may have been descended from a noble Phoenician family, but the current scholarly consensus is that Thales “was certainly a Greek and not a Phoenician” (Yust, 1952). Aristotle referred to Thales as being the first philosopher in the Greek tradition (Smith, 1870). Thales is often referred to as the Father of Science (Needham, 1978; Singer, 2008; Freely, 2012). The crucial contribution of Thales to scientific thought was that he was saying that the natural phenomena that surrounds all of us can be explained in terms of matter interacting by natural laws and are not the result of the arbitrary act by gods. He is credited with having initiated the practice of rational criticism of scientific theory in naturalistic terms (Lloyd, 1974). Thales’ hypothesis was that the nature of all matter was a single tangible material substance which he believed to be water. Simply put, he considered water to be the primal unit of matter, or arche. Thales was positing that everything in our world was derived from this arche. Aristotle wrote in his major work *Metaphysics* that Thales, the founder of the Meletian school of philosophy, was saying that the permanent entity is water. and derived this assumption from seeing that the nutriment of everything is moist, and that heat itself is generated from moisture and depends upon it for its existence. He derived his assumption from this and from the fact that the seeds of everything have a moist nature, whereas water is the first principle of the nature of moist things. Thales died in circa 548 BC (Cohen, 2000).

3.1.3 *Anaximander, Anaxagoras, Diogenes of Apollonia, Pythagoras*

Anaximander (611 BC-545 BC) was born in Miletus and was a student of Thales. He demurred from his mentor in that he believed that water could not be the arche because it could not give rise to its opposite, namely, fire. He theorized that some unknown substance or force was responsible. He called this theoretical substance *apeiron* (infinite). He said that this *apeiron* existed in two different forms, namely hot and cold,

and when they intermixed, they gave rise to the natural elements of, earth, water, air, and fire (Kocandrie, 2020).

Anaxagoras (570 BC- 500 BC), who came from Clazomende (in northern Iran) was a student of Anaximander and contributed a different theory of the understanding of the natural phenomena by saying that it was not water or *apeiron*, but air which was the main force of life (Curd, 2009). He expressed his views mainly through his teachings on astronomy. Diogenes of Apollonia (c460 BC-? BC) was a contemporary of Anaxagoras and was saying that it was not air but the heat of the fire given off by the *apeiron* that was the basis of all life (Curd, 2011).

Pythagoras (c570 BC-c490 BC) was born on the Greek island of Samos off the coast of modern Turkey. He was a philosopher and polymath who had a great influence on Plato and Aristotle. Unlike Thales, Pythagoras used ethics and religion as the basis for delivering his scientific principles (Burnet, 1930; Wright, 1995; Kahn, 2001). Pythagoras or his physician student Alcmaeon was the first philosopher to claim that the brain was the origin of the human intellect as well as the source of mental disturbances. He adopted an early notion of biological humor, or naturally occurring bodily liquids, as well as positing the concept of emotional temperament to aid in decoding the origins of aberrant passions and behaviors. He also believed in immortality and the transmigration of souls and made a serious effort to articulate the inner equilibrium of human anatomy and health. He was saying that the soul was composed of three parts: reason, intelligence, and passion” (Millon, 2004). It is believed that Pythagoras died in circa 490 BC, in either Croton or Metapontum in southern Italy (Riedweg, 2002; Huffman, 2005).

3.1.4 The Four Element Theory

The Greek philosopher Empedocles, born in c494 BC in Akragas, a Greek city in Sicily is credited in being the first to propose the Four Classical Elements Theory as a set namely earth, water, air, and fire. Some of his works survive, much of it in fragments (Wright, 1995). Empedocles posited that these four basic elements, which he referred to as “roots” (rhizomatic) made up all the structures in the world. This four-element

theory persisted as the standard dogma up to the Middle Ages and into the early modern period, when it became the object of experimental verification at the start of the scientific revolution and subsequently fell out of favour.

He is credited by most scholars as being the first to firmly establish the Four Element Theory of earth, water, air and fire. Some of his works survived, much of it in fragments (Wright, 1995). Empedocles was positing that these four basic elements, which he referred to as “roots” (rhizomatics) made up all of the studies of the world. In addition to the Four Elements, he added two further life “principles”, which became known as the concept of “love versus strife.” Empedocles argued that all of the four elements could combine in either a complementary or counteractive way. Should the combinations be complementary (attraction/love), then a harmonious result would exist. However, if the combination was counteractive (strife), then this would result in a personal breakdown or social disintegration (Kingsley, 2019). To Empedocles, blood was a perfect representation of an equal mix of fire, earth, air and water. He was saying that people’s problematic temperaments and mental disorders were due to imbalances within their own blood” (Millon, 2004).

Alcmaeon also had views on the nature of sleep, saying that this occurred when a person’s blood was withdrawn from their body surface to their deeper larger blood vessels and when the blood was returned to the body surface, then awareness occurs. If it did not, the result was death. Alcmaeon argued that physicians should only draw conclusions from empirical observations and experimentation - an idea that implicitly rejected the alternative notion that science should depend on “divine revelation” (Celesia, 2012).

Later Aristotle added a fifth element which he called *aether*, which he reasoned was the composition of all of the heavenly bodies and as such could not be constructed from earthly elements. Aristotle strongly criticized Empedocles and other philosophers who were associating *aether* with earthly fire.

The Four Element Theory persisted as the standard dogma up to the Middle Ages and into early modern period, when it became the object of experimental verification at the start of the scientific revolution before it subsequently fell out of favour.

3.1.5 *Four Humors Theory*

The concept of a Humoral Theory first surfaced in ancient Greece in the fifth century BC, although the original basic concept most likely dates to the Pharaohs in ancient Egypt (Abu-Asab et al, 2013) or possibly Mesopotamia (Sudhoff, 1926). However, the structural foundations for the theory were comprised of the extended work of the pre-Socratic Greek philosophers such as Pythagoras and especially the medical theorist Alcmaeon of Croton (c540 BC-c500 BC).

Following on from these philosophers, Hippocrates of Kos (460 BC- c370 BC) assembled these philosophers' ideas on the underlying four elements of nature, fire, water, air and earth and developed on the importance of hot, cold, wet, and dry to a person's health. He emphasized the significance of maintaining a balance in the body of these elements and established the foundation of the Four Humors Theory on the causation of human diseases (Yapijakis, 2009).

The fundamental concept of Hippocrates' theory relied heavily on there being four bodily fluids (or humors) that were thought to comprise the human body (Javier, 2014). These humors were believed to be influenced by changes in the environment such as the weather and the person's diet, and changes in these factors could produce various imbalances in a person's state of physical and mental health.

The Hippocratic Four Humors were: blood (hot and moist), phlegm (cold and moist), yellow bile (hot and dry), and black bile (cold and dry). These four humors were believed to exist in cycles, influenced by the seasons and the stellar constellations, revealing the strong influence of astronomy on the Hippocratic Humoral Theory.

For instance, an illness that occurred during winter was considered to be affected by an imbalance of phlegm within the body which could cause respiratory problems, whereas if the illness occurred during the summer months, it was an imbalance in the yellow bile, which resulted in a fever. The other two humors, black bile and blood were associated with the autumn and spring seasons. In order to balance the humors, treatments were based on the opposite. For example, to counter the overproduction of phlegm, which was associated with the cold of winter, such illnesses were treated with hot substances.

Gill noted the relationship of the Hippocratic Four Humors Theory to the earlier Four Element theory of natural elements: fire, water, air, and earth (Gill, 2013).

The Four Humors Theory provided a quasi-scientific premise of observation by the ancient physician, which was a major advancement compared to the proceeding earlier ideas, that relied heavily on superstition and mystical powers to explain the causation of disease (Javier, 2014). The Humoral Theory was strongly supported by Galen and remained unchallenged in Europe for many centuries, owing mainly to poorly established scientific knowledge during its existence. Ultimately, with the development of science and medicine during the Enlightenment era, the theory ended its long dominance.

3.1.6 Mental Health and the Four Humors

The Four Humor Theory allowed for simple explanations for complex emotional states. For example: when the blood humor (sanguinistic) was dominant, then such persons would experience “positive” emotions, such as joy and enthusiasm. However, when this humor was excessively abnormal, euphoria, obsessiveness and narcissistic tendencies would appear in such a person. When phlegm humor was dominant, a laidback (phlegmatic), good natured, sentimental personality is projected.

When there is an “imbalance” with this phlegm humor, then anxiety, fear, apprehension would appear. A person with a dominant yellow bile humor will exhibit an intolerant, demanding, caustic, irritable demeanor. Whereas someone with a dominant black bile humor will exhibit typical melancholic emotions, such as sadness, worry and pessimism. Furthermore, when the black bile humor is excessive, the depression, guilt and often panic are the dominant clinical features (Bhikha and Glynn, 2017). The issue of mental illness is examined later in this thesis, with a specific focus on the views of Asclepiades.

3.1.7 *Hippocrates of Kos*

Hippocrates was born on 460 BC on the Greek island of Kos (Cos) in the southern Aegean, as were his father and grandfather. Soranus of Ephesus (98 AD- 138 AD), the Greek physician and author was Hippocrates' first biographer. He is the source of most of the personal information about Hippocrates. Soranus was born in the ancient city of Ephesus (in modern-day Turkey) and practiced medicine in Alexandria and Rome (Drabkin, 1950).

Soranus said that Hippocrates learned most of his medicine from his father Heraclites as well as from his grandfather. This would have been in keeping with the practice of the day with Greek medical families. Soranus wrote that Hippocrates received his philosophical training at the Askleion in Kos. Some scholars have claimed that Hippocrates was a student of Democritus, although this has not been agreed (Kalachanis and Tsagkaris, 2020). Soranus said that Hippocrates took lessons in medicine from the famous Thracian physician Herodicus who is credited by many as the father of sports medicine (Berryman and Park, 1992). This has, however, been questioned by Helen King who draws attention to a set of fake letters ("pseudepigrapha") where it was claimed that no proof exists that Hippocrates had in fact corresponded with many of the famous historical figures that Soranus had claimed he had (King, 2006).

Hippocrates was widely respected as a physician. Plato referred to him as "Hippocrates the Asclepiad" and Hippocrates is frequently referred to as "the Father of Clinical Medicine". Hippocrates taught and practiced medicine throughout his whole life and travelled all over Greece, visiting Athens, Thessaly, and Thrace (Kiapokas, 2003). He most likely died at an advanced age, probably in c370 BC, in the ancient city of Larrisa in central Greece (Jones, 1923; Garrison, 1966; King, 2006; Nuland, 2008; Yapijakis, 2009).

Hippocrates is credited with being the first person to believe that all diseases occurred from natural causes and were not the wrath of gods or magical superstition (Garrison, 1966; Grammaticos and Diamantis, 2008). He was the first physician to separate the discipline of medicine from religion, arguing that disease was not a

punishment inflicted by the gods, but the product of environmental factors such as diet and general living habits. Before Hippocrates, therapeutic efforts were based largely on religious or magical beliefs, and medicine was commonly practiced by priests, spiritual healers, and witch doctors (Yapijakis, 2009).

Hippocrates had based his humoral approach to medicine on the earlier philosophical theories of Pythagorean philosopher Empedocles (493 BC-433 BC). His belief was that human health was maintained by the harmonious balance of the Four Fluid Humoral Elements, as well as the other four elemental conditions of cold, hot, dry and moist.

Hippocrates based his medical approach on what he called the “healing power of Nature” (*vis mediatrix naturae*). According to this doctrine, the human body contains within itself the power to re-balance the Four Humors. Health, according to Hippocrates, existed when these four humors were in harmonious balance. In human disease situations, the physician’s aim was to correct the imbalance of the altered ratio of the four humors in order to facilitate the work of a “Benevolent Nature”. Some scholars believe that Hippocrates was influenced in his medical thoughts by Herodicus’ earlier theory of disease causation, which Herodicus said was due to an imbalance of sharp and bitter liquids in one or more of human internal organs (Berryman and Park, 1992).

According to Hippocrates, the physician’s first approach was to carefully take a detailed medical history from the patient and follow this with a careful full medical examination. At the same time, the physician would observe and record all clinical signs and then make a diagnosis. This ancient Hippocratic approach established the foundations of current clinical medicine as it is practiced today (Edelstein, 1967; Kiapokas, 2003; Yapijakis, 2009). Hippocratic therapies set out to achieve a balancing correction of humors by the use of various treatments that included: bloodletting, emetics, purgatives, herbs and occasionally surgery depending on the particular disease.

For example, Hippocrates felt that it was too much phlegm that caused epilepsy; too much black bile caused melancholy; and mental illnesses in general were described as caused by too much moisture on the brain. One of the strengths of Hippocratic

medicine was its emphasis on a “prognosis”. However, the only meaningful thing that a Hippocratic physician could provide to his patient was to evaluate their illness and predict its likely progress, based upon signs and symptoms that had previously been collected and listed by other physicians in detailed medical case histories.

The seventy or so texts, which are known as the “Hippocratic Corpus”, date mostly from around 420 BC to 370 BC (Wellman, 1929; King, 2006). This assorted group of early Greek medical treatises of very different types were brought together by a variety of different people, at different times, probably at the beginning of the third century BC. Most of these texts were deposited in the great library in Alexandria Egypt (King, 2006 and 2011). The question as to whether Hippocrates was the author himself of any, or some, of the treatises within the Corpus, has never been conclusively answered. Because of the different writing styles and apparent different dates of construction of the Corpus, it has been generally agreed that the Corpus could not have been written by any one person (Singer and Underwood, 1962).

The Hippocratic Corpus covers many diverse aspects of medicine, ranging from medical causation theories to the appropriate ethical means of medical practice. Many different illnesses are described, in varying degrees of detail, which supports the likelihood of there being many different authors writing, at different times, which ultimately contributed to the construction of Corpus. Some of the treatises are substantial works while others are short pieces. Some of the texts give grand theories of the nature of the body and origin of disease, while others give simple recipes for remedies or basic advice on how to bandage a wound (King, 2006).

At various points, the Hippocratic Corpus mentions patients presenting with clinical signs and symptoms that would be consistent with current day presentations of various medical conditions. References are made to mania, the general Greek term for madness (“insanity”); melancholia (“depression”); phrenitis (“delirium”), a condition of the mind that was originally thought to originate and exist in the diaphragm. In the Corpus, the senses were not precisely determined, and the concept of mental illness, as a separate disease entity, was not closely fixed. People did present with delusions, hallucinations, and general bizarre behaviors, and while not specifically identified as a

specific condition, Kauffman and McLennan concluded that schizophrenia did exist as a discrete concept in Greco-Roman classical times (Kauffman and McLennan, 2017).

The Hippocratic school of medicine revolutionized ancient Greek medicine for generations and established medicine as a discipline that was distinct and separate from other fields (Nuland, 2008). As Yapijakis notes “Hippocrates’ contribution to medical practice is characterised by his ethical rules of conduct, close observation of clinical symptoms, an open mind for any ideas and a willingness to explain the cause of diseases, much of which is still applicable to the modern physician” (Yapijakis, 2009).

3.2 The Philosophical History of the Greek Particle Theory of Matter

The nature of matter and the idea of invisible particles has fascinated philosophers, historians, and medical scientists from antiquity to the present day. The philosophical history of the Greek particulate theories on the constitution of all matter is both long and distinguished. Groups of pre-Socratic philosophers, which initially included Thales of Miletus were starting a long tradition of attempts to try and explain nature by using experience based on the senses, as well as imagination, based on empirical analysis and random thought (Whyte, 1960; Farrington, 2000; Yapijakis, 2009).

3.2.1 *Leucippus and Democritus*

In the fifth century BC, two Greek philosophers, Leucippus and his pupil Democritus, attempted to explain complex phenomena based on a particulate (solid) theory, as an alternative to the humoral (liquid) theory that had been postulated by Hippocrates (Berryman, 2009). These philosophical theorists put forward a revolutionary theory of matter contending that all of the material universe was made up of minute undetectable and indivisible particles which they called atoms or *atomoi*. The word atom comes from the Greek word *atomos* (which means “indivisible” or “uncuttable”). Leucippus and Democritus were positing that all the basic elements of matter consisted of such atoms

which were of various forms and shapes. These atoms accounted for all the observed differences in all matter. They were claiming that it then logically follows that any changes in the observed appearance or difference of all matter must therefore be due to changes in these minute invisible atoms (Wellman, 1929; Horne, 1963; Zigioli, 2021). Traditional atomism has been used in two distinct domains: the atomism of physical science and the atomism of philosophy. It is generally accepted by most scholars that Leucippus and Democritus were the Fathers of Philosophical Atomism (Burnet, 1930).

Leucippus is a somewhat vague figure. Nothing is known of his life. Epicurus even doubted his very existence. While it is generally agreed that he was born around 460 BC, there is scholarly debate as to where he was born. Burnet was of the view that it was most likely in the ancient city of Miletus, on the western coast of Anatolia, in modern-day Turkey (Burnet, 1930). However, other scholars have suggested that he was born in Abdera in the Thrace region of Greece or possibly even in Elea, a city founded by the Greeks in modern day Italy. No written word by Leucippus has survived and the date of his death is not known (Barnes, 1984; Berryman, 2009). Aristotle and his pupil Theophrastus (c371 BC-c287 BC) explicitly credited Leucippus with being the inventor of the theory of Atomism (Burnet, 1930). Unfortunately, Aristotle is not consistent in his various references to Leucippus. He sometimes suggests that atomism began with Leucippus, while at other times he links Leucippus with his most famous pupil Democritus, and even in a few places Aristotle seems to imply that Democritus alone invented atomism. In addition, it has proved to be difficult for scholars to distinguish between the views of Leucippus and his better-known pupil Democritus, as their atomistic views became so intertwined as to be almost indistinguishable. However most agree that Leucippus, in conjunction with Democritus together founded the famous Philosophical School in Abdera Greece (Kirk and Raven, 1957).

Democritus (460 BC-370 BC) was born in Abdera in the Thrace region of Greece. He put forward an atomic theory which stated that fundamentally there are only two basic kinds of realities composing the natural world, namely atoms and voids. He claimed that these atoms were solid, infinite in number, of various sizes and shapes as well as being indivisible and they moved about in perpetual motion. He theorized that, in order to move about, these atoms required the presence of an infinite space

which he called a void. Within this infinite void the atoms could move around freely, repelling and colliding with each other and combining to form the many different complex components that ultimately led to the composition of the entire universe (De Witt, 1932; Berryman, 2004; Brancaccio and Morel, 2007). What Democritus was postulating was a purely mechanical materialism which was devoid of any trace of the mystical, which was a very rare proposition in Greek philosophy at that time. He argued that all phenomena, both physical and spiritual, could be explained by this theoretical mechanistic reality of matter (De Witt, 1932). However, it is of some interest to note that Democritus was still alive when his new “scientific movement” suffered a significant reverse. As Norman De Witt said “it was in Athens, a center of conservatism that the opposition to atomism arose, and the intellectual revolt was brilliantly led by Socrates, who despaired of the possibility of a “scientific knowledge” developing. Even Aristotle, who pioneered in some branches of science, was also rejecting the atomic theory of matter. Between these two great names came that of Plato who was postulating a purely mathematical theory, saying that the ultimate realities of all matter were geometric micro-structures such as “triangles, cubes, spheres and the like” (De Witt, 1947). Importantly, it that should be noted that Aristotle was also a believer in a divine controlling power of the eternal universe which ultimately made his philosophical teachings acceptable to Christianity, as in the writings of Thomas Aquinas (Artmann and Schafer, 1993).

3.2.2 Socrates, Plato, Aristotle

Socrates (470 BC-399 BC)

Socrates was born in Athens and was the pivotal figure in Greek thought. Philosophy before him is often referred to as pre-Socratic. He lived for 70 years before meeting his well-known death by drinking hemlock in 399 BC (Gutrie, 2008). Socrates claimed

that true knowledge could only be obtained by analyzing concepts. He promulgated the power of reason, stating that it was only through rational processes that one could discern that which is both objective and universal. He said that a life without thoughtful discourse would “be unworthy of a man” (Durant, 1953). It is notable that Socrates wrote down nothing tangible himself. His thoughts and ideas have come to us through recorded dialogues which were written by his famous pupil Plato. According to Socrates, “ignorance was not even a consequence of a lack of technical knowledge, but a lack of knowledge about one’s inner mental life”. “Know thyself” was a guiding principle, and “knowing that one knows was an even higher principle” (Millon, 2004). Nevertheless, Socrates claimed in his Apology “all I know for sure is that I know nothing”, a phrase that some (like Plato) explained in the sense that the human wisdom is limited compared to divine limitless wisdom, while others (like Lucian) took it literally and accepted that indeed Socrates did not know anything because he used the wrong dialectic method to reach knowledge instead of objective observation and analogical inference.

Plato (429 BC-347 BC)

Plato was born in Athens and had great admiration for his mentor Socrates whom he had often heard speaking in public debates. After Socrates’ death in 399 BC, Plato travelled all over the Mediterranean, and especially in Sicily where for several years he acted as adviser of tyrants of Syracuse, before returning to Athens in 387 BC, where he established his own famous school which was known as the “Academy”. Plato, like Hippocrates before him, believed that the human body was composed of the Four Humors. However, he took this stage further by saying that human development progressed in a manner as described by Democritus in his materialism theory of atoms and void. Plato was both a humorist and an atomist (De Witt, 1932). In his famous *Timaeus* (dialogue), most likely influenced by the Geometric and Number Theory of Pythagoras and based largely on the Four Element Theory of Empedocles, Plato identified each of the four natural elements with a perfect mathematical form: fire (with an Aetrahedron), air (with an Octahedron), water (with a Cosahedron), and earth (with

a Cube). He then divided the face of each of these solids into what he called “Elemental Triangles” of new materials (Berryman, 2004). Plato was putting forward a theory that all matter, including the human body and the universe, as well as our world, was composed of the four elements, as well as various types of three-dimensional geometric triangular shapes, which were the ultimate unchanging reality. However, it must be remembered that Plato was not an atomist. In fact, he argued against the emerging Atomists saying that “atoms could never produce the form of beauty of the world” (Lloyd, 1974). Plato’s philosophy has greatly influenced the basic dogmas of Christianity, especially during the medieval era.

Aristotle (384 BC-322 BC)

Aristotle (384 BC- 322 BC) was born in Stagira in Northern Greece. Little is known about his early life. His father Nicomachus had been a court physician in Macedon and had been trained in scientific observation from his youth. Both his father and his mother both died when he was a child, and he was brought up by a guardian. He left his home to go to Athens when he was about 17 years of age to join Plato’s Academy. He remained Plato’s student for almost twenty years and built up a vast personal library. After Plato chose his nephew Speusippus (408 BC-339 BC) to be his successor in the Academy. Aristotle subsequently left Athens in 343 BC at the request of King Philip II of Macedon, to become the tutor of the King’s son Alexander, who later became known as Alexander the Great (Shields, 2022).

At the age of 53, Aristotle returned to Athens where, for reasons which are not entirely clear, he was again denied the leadership of the Academy. He was very disappointed about this and subsequently established his own rival philosophical school which he called the “Lyceum.” While his mentor Plato loved mathematics, Aristotle’s main interest was in science and especially in biology. The Lyceum soon became the major center for scientific study. Aristotle’s Lyceum continued to function and flourish under a series of leaders, until the Roman general Sulla, during his assault on Athens, destroyed it in 86 BC (Lynch, 1972).

Aristotle's philosophical as well as his scientific observations and conclusions were to be unsurpassed up to the time of the Renaissance. Although he had been a student of Plato's for over 20 years, Aristotle turned sharply away from Plato's teachings and towards his own views that were more realistic and tangible than the abstract and idealistic ones put forward by his master. As Aristotle was more of a scientist than a philosopher, he gave special attention to the need for empirical verification and sensory based observational data. In contrast to Plato's Academy, the teaching in the Lyceum focused more on biology and the natural sciences, than on mathematics and political philosophy, which were the main academic areas of interest for students of the Academy (Millon, 2004). Agreeing with Empedocles, Aristotle believed that the world consisted of the Four Elements of: earth, water, air, fire. Like his mentor Plato, Aristotle rejected the Atomic Theory of Matter. While not a supporter of the emerging Democritian atomic theory, his objections were more measured than those of Plato (McMullin, 1965). While agreeing with the Four Element Theory that had been espoused by Empedocles, Aristotle went further, theorizing that the four elements could interact with each other and be transformed into different substances, an idea that may have subsequently fueled the future search throughout the Middle Ages for the so-called "Philosophers Stone". Aristotle developed Socrates' "ideal form" into a theory which aimed to explain existence through the composition of matter and form. He conceived a theory of matter that espoused as a passive possibility that something might be actualized by an "acute principle" a substantial form giving all matter its real existence. However, Aristotle's theory of matter, which was known as Hylomorphism, had little impact on the ancient world of his time.

3.2.3 Herophilus (335 BC-255 BC) and Erasistratus (304 BC- 250 BC)

An important Greek physician of the Hellenistic era was Herophilus. He was born in Asia Minor (now Kadiköy, in modern day Turkey). Very little is known of his early life, but it appears that he travelled at an early age for his schooling in Alexandria. He is credited by many for being the first physician to perform dissections on human cadavers. He recorded his findings in eleven treatises that unfortunately are lost, most

likely in the great fire of the Alexandrian library (Wills, 1999). Many have claimed that he also performed vivisections on living human prisoners. He is generally regarded by most scholars as being the Father of Human Anatomy (Dobson, 1925; Wiltse and Pait, 1998). He is believed to have been the first to differentiate nerves from blood vessels and tendons, and to realize thus nerves carried neural impulses (Longrigg, 1972; Wiltse and Pait, 1999). Both Herophilus and Erasistratus appreciated that there were two types of nerves, motor and sensory (Rocca, 2003).

Erasistratus was born on the Greek island of Ceos and was a notable and distinguished Greek physician and anatomist. Very little is known of his early life. He most likely studied in Alexandria, which at that time was beginning to becoming a celebrated medical school (Lloyd, 1975). He is credited, along with his physician colleague Herophilus, in founding the famous anatomical school of anatomy in Alexandria. Erasistratus continued and elaborated on the research which his colleague Herophilus had started. He was the first to describe the valves of the heart and that it acted as a pump. He said that arteries carried air which he called the vital pneuma, and that this pneuma travelled through hollow nerves. In conjunction with Herophilus, they made the distinction between sensory and motor nerves and linked both to the brain. Erasistratus gave detailed descriptions of the cranial ventricles and meninges and said that it was the brain, not the heart, that was the seat of human intelligence. This was in direct contrast to Aristotle who had believed that it was the heart and not the brain (Grmek and Fantini, 2002).

Erasistratus and Herophilus are also credited by most historical scholars and medical historians as being the Fathers of Physiology, especially Neuroscience. Erasistratus was also the first major exponent of the Theory of Pneumatism, which was based on the premise that all life is associated with, and sustained by, a subtle vapor that he called the vital pneuma (Wilson, 1959). Von Staden is of the view that Erasistratus' approach to anatomy and physiology was essentially Aristotelian (von Staden, 1997).

Erasistratus had a view that there was a "triple web network" at work in the human body: the veins (from the heart's right ventricle), the arteries (from the left ventricle), and the nerves (from the brain's meninges) (Leith, 2015 and 2020).

Erasistratus adopted Herophilus' view that the psychic pneuma in the nervous system was responsible for both mediating sensory sensations, originating in the meninges as well as motor movement, originating in the cerebellum (Leith, 2020). Both Erasistratus and Herophilus had also come very close to working out the mechanics of the human cardiac circulation which was not accurately discovered until William Harvey did so in 1628 (Harvey, 1628).

While in Alexandria, Erasistratus in conjunction with Herophilus are credited, in helping to lay down the foundation of the Empiric School of Medical Teaching. This medical teaching approach opposed the traditional humoral approach of the Hippocratic ideologies (von Staden, 1997).

3.2.4 *Epicurus (341 BC-270 BC)*

Epicurus was one of the most famous of the Greek philosophers. He was born to Athenian parents Neocles and Charrestrate in 341 BC on the Greek island of Samos, or possibly as some believe, in Athens (Bailey, 1928; DeWitt, 1932; Wilson, 1959). His academic philosophy teachers were Pamphilus while he was in Samos, and Xenocrates while he was in Athens (Yapijakis, 2022). He had an extensive liberal education in his youth. He studied philosophy with several teachers including a Platonic, an Aristotelian and a Democritean-Skeptic, with his teachings being heavily influenced by the earlier Greek philosophers, particularly Democritus and Aristotle. During his lifetime Platonism was the dominant philosophy in higher education. However, Epicurus' opposition to Platonism formed a large part of his thinking throughout his life (De Witt, 1932).

After the death of Alexander the Great in 323 BC, Athenian settlers were expelled from Samos by Perdiccas. Epicurus subsequently went to Athens when he was 18 years of age but after a short stay, he left Athens to join his father in Colophon, a Greek city situated close to the ancient city of Ephesus (in modern-day Turkey). Here he is purported to have studied atomism under the tutelage of the Democritean philosopher Nausiphanes (c325 BC-c290 BC). However, he fell out with Nausiphanes and subsequently moved on to Mytilene on the Greek island of Lesbos and from there to

Lampsacus in Bithynia, where in 310 BC he founded his own philosophical school, before finally returning to Athens in 306 BC.

Epicurus was a strong believer of the atomic theory of matter (Wilson, 2015). In Athens, he continued to study the atomic philosophies of Democritus and Erasistratus, while always conscious of Aristotle's arguments against atomism (Yapijakis, 2009). Epicurus subsequently formed his own philosophical school in Athens. He situated his school in the garden of his own house, which was situated outside the city walls, near the *dipylon*, also known as the double gates (Yapijakis, 2022). Epicurus' unique school became famously known as the Garden of Epicurus, or the *Kepos* (De Witt, 1932; Yapijakis, 2022). The essential goal of Epicurean philosophy was for people to attain a happy and tranquil life, characterized by the absence of pain and fear (De Witt, 1947; Englert, 1987; Avradmides et al, 2000; Yapijakis, 2013, 2016 and 2022). The *Kepos* provided students with an environment of intellectual freedom that allowed for scientific medicine to be born.

Epicurus realized that he needed an explanatory basis for the understanding of the physical world, and for that purpose, he selected the atomism of Democritus (De Witt, 1932; Bergsma, Poot and Liefbroer, 2008; Yapijakis, 2017). In establishing his own particulate theory, Epicurus combined the physical atomic theory of Democritus with the naturalistic ethics of Aristotle. Epicurus evolved atomic physics in response to Aristotle's criticisms of Democritean theory, by using his methodology of Canon which involved observation with the senses and inference by analogy, Epicurus agreed more with Aristotle whose empirical method he used and whose positions regarding chance and free will he accepted distancing himself from earlier atomist Democritus (Yapijakis, 2017). Epicurus introduced his own theoretical concept of infinite and indivisible atoms which were continuously moving about in an infinite void. He suggested that these atoms were combining by "necessity and chance", to form larger bodies which he called molecules (De Witt, 1932). He claimed that these atoms and molecules lay within a void space and formed the basis of all the matter within the entire physical world.

Importantly, he was saying that "his atoms" were the basis of all evolving living organisms including the human body (DeWitt, 1932; Inwood et al, 1994; Yapijakis,

2009; Leith, 2023). As Yapijakis has pointed out: “Epicurus believed that the eternal Nature consisted of atoms and void space and that the sum of all matter was conserved. He was positing that these atoms were perpetually being used by necessity and chance only and were in an endless process of construction and decay of all material objects” (Yapijakis, 2009).

Epicurus tried to free people from superstition and unsubstantiated fears of the unknown. He believed that gods exist as blissful and eternal entities composed by atoms. He was saying that objective observation of the cosmos suggests that gods do not care about the universe or humans. Therefore, humans should not fear gods or expect favors from them and true piety for mortals is the admiration of the divine nature and the strive to imitate gods’ happiness in life. Epicurus was a materialist, stating that death destroys all souls as well as the senses. He argued that because there is no destiny (i.e., no determinism) and because of the existence of chance as atomic movements permit free will in people (Inwood et al, 1994). Epicurus’ essential message was, “that all people may achieve happiness if their way of living, and that this is based on prudence, virtue, justice, friendship and objective knowledge” (Yapijakis, 2009). Several enlightened Christian humanists in the late Renaissance recognized common elements in the humane ethics of Epicurus and Jesus, such as the free will and the promotion of friendship/love among people. Such people included the Italian Lorenzo Valla, the Englishman Thomas More, the Dutch Desiderius Erasmus and the French philosopher, astronomer and Catholic priest Pierre Gassendi, who revived Epicurean philosophy reconciling it with Christianity (Yapijakis, 2022).

The complex relationship between Asclepiades and Epicurus is dealt with later in this thesis (4.1.2).

3.3 Medical Practice in Ancient Rome

Little is known about the practice of ancient medicine in early Rome as there is no Roman equivalent of the Hippocratic corpus. Most of the medical treatments carried out at that time in Rome were largely being performed within the family circle, based on the authority of the male head of the household, known as the “pater familia” or

patriarch (Allbutt, 1921). Such treatments mainly involved the patient taking various vegetables and herbs. Magic formulas, priestly interventions as well as invoking the healing gods were also common practices. Some of the wealthier families had their own physicians, who was usually one of their slaves or a “freed” slave (Santacroce et al, 2017). Most of the Roman populace were generally suspicious of physicians who worked for a fee. Roman civilization was not too concerned with abstract concepts and there appears to have been very little interest in theoretical medicine. The Romans were largely a pragmatic race, being accomplished engineers, builders, and lawmakers.

Although Asclepiades lived in a period where Greek doctors were a familiar feature of the Roman medical scene, Pliny the Elder believed that a medical profession was not really necessary, arguing that “Nature herself has provided for all the remedies we need...but Earth is kind and gentle and bountiful ever a hand maiden in the service of mortals” (Pliny, N.H. 2.155). Even so, medical doctors who could treat war wounds and war injuries were in great demand by the Roman army and their naval fleet (King, 2006). Army hospitals were built in the fortresses along the Roman borders and the role of a soldier-medical in the Roman army was gradually developed. Military medicine was almost exclusively confined to wound injuries in field hospitals that were known as *valetudinarians*, with the surgery being performed by these soldier-medics. The variety and nature of the surgical instruments which were discovered in ancient Roman archaeological sites indicated that these soldier-surgeons had a sound knowledge of the practical surgical management of wounds (Byrne, 1910, Bröckmann, 2005).

According to Pliny the Elder there were no real medical doctors as such in Rome before the arrival in 219 BC of the so-called “first Greek doctor in Rome”, the Peloponnesian immigrant Archagathus of Sparta, son of Lysanias [Pliny NH 29.12-13]. Little is known of the history of Archagathus before he came to Rome. However, on his arrival in Rome he was welcomed and was given the right of Roman citizenship (*Jus Quiritium*) as well as his own workshop (*taberna*) which was situated in the *Compitum Acilli* (crossroads) in Rome.

At first, Archagathus had a very successful practice being called the “wound-man” or *vulnerarius*. This was an appropriate skill for a doctor to have at this time in Rome considering that the Second Punic War with Carthage (a former Phoenician city-

state in present-day Tunisia) was about to erupt with Hannibal having already crossed the Alps in 218 BC (Terrell, 1922; Conrad, 1995). According to Pliny, Archagathus soon lost his initial popularity in Rome and public opinion turned against him after he introduced his primitive surgical methods to his work. He was subsequently renamed “the executioner” or *carnifex* because he purged, bled, hacked, and cauterised his patients to such a degree that eventually the sick citizens of Rome refused to tolerate any longer his rough and barbaric treatments (Pliny NH, 29,6, 12-14; Turner, 1736; Curry, 1856; Nutton, 2005).

Cato the Elder (234 BC- 149 BC), also known as Cato the Censor. He was a Roman soldier, senator, and historian, and another key figure in the history of Rome of this time. He was noted for his conservative views. He was devoted to agriculture and to military service. He was vitriolically opposed to all things Greek, especially when it came to Greek medicine. He was born into an ancient traditional Plebeian family which was well known for their military service to Rome (Scott, 1955). He spoke of the Greeks as “a scoundrel and incorrigible race,” saying that when the Greeks give us their writings they will corrupt everything, all the more if they send their doctors (Scott, 1955). Cato was not a physician himself, but in the true tradition of the *pater familia*, he practiced medicine in his own household, believing, among other things, that cabbage was the universal remedy for most illnesses and diseases. The historian Cassius Hemina wrote in his Annals in 150 BC that Cato had made a political career out of his strident hostility to all things foreign, especially to Greek medicine (Hemina). Pliny said that Cato had notebooks of his own that contained various prescriptions and recipes, and probably also had magic charms (Pliny, NH 29,12-15; Rawson, 1985). Pliny later added to this by quoting Cato as saying, that “the Greeks vow amongst themselves to kill all barbarians with their medicines, which they perform for pay in order to increase our trust and easily destroy us” (Pliny NH, 29,10; Gruen, 1992).

Both Cato’s and Pliny’s invective against Greek physicians might have been due to a misunderstanding of a story referred to in Plutarch’s “Life of Cato”, where it is mentioned that Hippocrates had taken an oath “not to serve barbarians who were the enemies of Greece”. In any case, their positions were relevant to the life and work Asclepiades of Bithynia, who forms the focus of this thesis.

3.4 The Life and Death of Asclepiades of Bithynia (124 BC- 40 BC)

Asclepiades of Bithynia was the first leading representative of Greek theoretical medicine to work in Rome in the late second and early first centuries BC (Yapijakis, 2009; Leith, 2020). His influence continued up to 164 AD, until Galen began to practice medicine in Rome (Brady and Kelly, 2022). This account of life and death of Asclepiades is based on sources discussed in Chapter 2 of this thesis.

3.4.1 *Asclepiades' Early Life*

Antonio Cocchi (1695-1758), the noted Italian classical scholar and physician, wrote that, in Ancient Greece, many of the most effective physicians maintained some association with the national religion, either through affiliation with a temple to Asclepius or by assuming a name that was related to the mythical god of medicine. Therefore, scattered through ancient Greek history there have been many men bearing the patronymic “Asclepiades”.

In 1758, Cocchi published his famous work on Asclepiades, called the *Discorso Primo Sopra Asclepiade* (Cocchi, 1758). Cocchi estimated that there were about 40 men with the cognomen Asclepiades, whereas Gumpert (1772-1832) the noted Polish historian physician and author counted only 10 men called Asclepiades (Gumpert, 1794). Regardless of the actual number, only three of this group stand out. First, there was Asclepiades Pharmacion, who was a pharmacist and not a physician and was a contemporary of the two Emperors, Nero (37 AD-68 AD) and Domitian (51 AD-96 AD). Second, there was Asclepiades Myrleanus who came from the region of Myrlea in Bithynia. He also was not a physician but was a noted teacher of grammar and rhetoric and was in Rome in the time of Pompey (106 BC-48 BC).

It is generally accepted that the most prominent and distinguished of these three men was the third figure, Asclepiades of Bithynia, who was the first physician to firmly

establish Greek medicine in Rome (Cocchi, 1758; Edelstein, 1967; Rawson, 1982; Porter, 1996; Yapijakis, 2009; Brady and Kelly, 2023). Historically, Asclepiades stood at a crucial point in the development of Greek medicine, placed between the great third century Greek doctor Erasistratus and Galen of Pergamon. Rawson writes that “there was no intellectual figure at work in Rome in the period of the late Republic who had more originality and influence than the Bithynian doctor Asclepiades” (Rawson, 1982).

Asclepiades was born in 124 BC in the seaside port town of Prusias-on-Sea (*Prusias-ad-Mare*), also known as Cianus or Cius. This ancient town was situated on the Bithynian shore of the Propontis (now known as the Sea of Marmara), close to the modern Turkish city of Gemlik, in the Bursa Province of Northwestern Turkey. Asclepiades lived there around three centuries after Hippocrates and around two centuries before Galen (Yapijakis, 2009; Flemming, 2012). It was a town of little independence and did not mint coins. However, its loyalty to Rome earned Bithynia its “freedom”, when in 74 BC the area was turned into a Roman province. Rawson “wonders if this loyalty to Rome anything had to do with the great success in Rome of its most distinguished son” (Rawson, 1982).

Very little is known of Asclepiades early life. None of his own writings remain except for certain fragments (Gumpert, 1794). It is not entirely clear if he came from a medical family, which would have been in keeping with the Greek practice of the day. Polito explored Asclepiades’ chronology and concluded that his father may have been the physician Andreas of Carystus, an ancient Greek city state on the island of Euboea also known as Evia (Polito, 2006 and 2007). Andreas spent most of his life in Alexandria and was a follower of Herophilus, the famed Greek anatomist. He was a physician to Ptolemy Philopater, King of Egypt. Andreas was killed (probably assassinated) in 217 BC just before the battle of Raphia, which is situated in modern day Syria (von Staden, 1989). However, the name Andreas was a fairly common name of several physicians in ancient Greece and as a result it has proved to be difficult to distinguish one from the other. Polito concluded that there was a possibility that Asclepiades could possibly have been born to the physician Andreas when he was living in Alexandria (Polito, 1999). Having fully explored this possibility, Rawson

concluded that it was most unlikely that Andreas of Carystus was the father of Asclepiades of Bithynia (Rawson, 1982).

Cocchi said it is most likely that Asclepiades had a good education as a youth when he was living in Bithynia, as his home was adjacent to the two great Kingdoms of Mysia and Phrygia, both of which had famous schools of learning in oratory, history, philosophy, and mathematics (Bowie, 2014). Cocchi added that it appears from his remaining fragments, that Asclepiades spoke the Attic dialect, the characteristic of which was style and clarity and that Asclepiades, “from his exact manner of deducting the necessary conclusions from his premises, in which Galen himself says, that he (Asclepiades) was excellent” (Cocchi, 1758; Galen, *Concerning the Natural Faculties*, lib1, tom,1). However, Raynaud has said that much of what Cocchi has said in relation to Asclepiades’ early education in Bithynia and possibly in related areas is highly speculative and goes on to say that it appears that Cocchi was endeavoring to embellish the virtues of Asclepiades (Raynaud, 1862). Rawson has also said that in Cocchi’s discords on Asclepiades, that while he (Cocchi) “is learned and often penetrating, through over-enthusiastic about his subject’s (Asclepiades) moral virtues” (Rawson, 1982).

Asclepiades appears to have remained in Bithynia until he was around 20 years of age before travelling widely and continuing with his studies until he was around 30 years of age. At some point during his travelling period, Asclepiades attended the Epicurean school at the *Kapos* in Athens (Cael. Aur., Cel. Pass.2.22.129). There, he was able to obtain further knowledge in the various systems of Greek philosophy (Cocchi,1758). During his philosophical training at the *Kepos*, and like so many other students who were studying there, he was greatly influenced by the Epicurean philosopher Zeno of Sidon (a city in modern day Lebanon), who was the leader of the Athenian *Kepos* at that time (Cocchi, 1758; De Witt, 1932; Yapijakis, 2009). Underscoring the intellectual link between philosophy and medicine, Zeno taught that philosophy was, “the medicine for the soul” (Tsouna, 2007).

3.4.2 *Turning to Medicine*

Following on from his philosophical learning period Asclepiades started to take a great interest in medicine and medical matters. He travelled widely, visiting many of the great medical schools of the time, including the famed Asklepion school in Pergamon with its great library. The ancient city of Pergamon is now also known as Bergamon in modern day Turkey (Cocchi, 1758; Gumpert, 1794 ;). Some scholars have claimed that he may have obtained further medical education and training at the famous medical school in Alexandria which had a famous Anatomical School (Wellman, 1908; Allbutt, 1921; Yapijakis, 2009; Santacroce et al, 2017). However, Flemming doubts this stating that “whether Asclepiades ever visited Alexandria is unclear” (Flemming, 2012).

Asclepiades’ relative ignorance of human anatomy, highlighted by both Pliny (NH.26.12) and Galen (De Fac. Nat.3.7.166), seems to suggest that he had not studied in Alexandria. In any event, due to his interest in theoretical principles, anatomy was not of great importance to Asclepiades (Rawson, 1985). Leith is of the view that “there is no evidence, and no good reason to believe, that he ever went to Alexandria” (Leith, 2021).

Asclepiades most likely first practiced medicine in the ancient famous Greek maritime city of Parium in the Kingdom of Mysia, which was situated in the Hellespont region (modern Dardanelles), on the northern coast of modern-day Turkey. After spending some time in Parium, he journeyed through Hellespont and appears to have returned to Athens where he continued with his medical practice for several years (Cael. Aurl. Cel.pass.2.22.129; Leith, 2009). He subsequently decided to go to Rome where he remained for the rest of his long, illustrious life (Caelius Aurelianus; Rawson, 1982; Yapijakis, 2009; Leith, 2021).

3.4.3 *Asclepiades in Rome*

It is interesting to reflect as to why Asclepiades chose to go to Rome at this stage of his career. Flemming speculates that Asclepiades’ choice of the emerging metropolis as his base, at the expense of Alexandria, which was at the time the established medical center of the Mediterranean may have been due more to the fact the Egyptian capital was less philosophically developed than Rome (Flemming, 2012). In any case,

Asclepiades arrived in Rome when he was about 30 of age and, according to Gumpert, he was already an experienced physician (Gumpert, 1794). It is generally agreed that he initially taught rhetoric and philosophy on his arrival in Rome, before commencing what was to prove to be a highly successful medical practice (Rawson, 1982; Yapijakis, 2009; Leith, 2020). When Asclepiades arrived first in Rome there existed a significant climate of suspicion and hostility towards Greek doctors, generated in large part by Cato the Elder (see above). As already mentioned, Asclepiades was not the first Greek doctor to arrive in Rome to start a medical practice; that dubious honor belongs to his fellow countryman Archagathus. However, it is generally agreed by most scholars that Asclepiades was undoubtedly the first major authority in theoretical medicine to become established in Rome (Rawson, 1982; Leith, 2020). As Raynaud points out “Although a long span of time had elapsed between Archagathus and Asclepiades’ arrival in Rome, he [Asclepiades] still found that the legacy and former image of Archagathus was impeding him”. So (this) may have been the reason that “Asclepiades pursued a different path and an entirely different persona...whether in gentleness or careful manners as well as with humane and pleasant treatments he soon surpassed all other doctors in Rome” (Raynaud, 1862).

Asclepiades’ knowledge of medicine and philosophy, coupled with his considerable rhetorical skills and personality, allowed him not only to flourish as a physician, but to be accepted into the intellectual and sophisticated aristocratic circles that existed in Rome during the late Republic period (Rawson, 1982; B.M.J., 1984; Alonso, 2018). Cocchi felt that it was likely that Asclepiades had been granted Roman citizenship or at least had been given the right of Roman citizenship under a section of Roman law known as the *Jus Quiritium*, just as Archagathus had been given it a hundred years before Asclepiades’ arrival in Rome (Cocchi, 1758 in Green, 1955). Cocchi noted there was no trace of Asclepiades of ever having adopted a Roman male citizen’s custom of adopting a cognomen (an extra personal name, or nickname) which most male Roman citizens took. As Cocchi said “Asclepiades retained his single name in the Greek manner, without needing, or caring to assume, through clientele or through other dependency, that of a Roman family, as many other Greeks had done before him” (Cocchi, 1758). Cocchi added that Asclepiades was much beloved and held in high

esteem by the most considerable personages in Rome and was content to be the humble friend of the powerful Roman senators. Yapijakis has said that he received the names Philosophicus because of his knowledge of philosophy and Pharmacion for his knowledge of medicinal herbs (Yapijakis, 2009). Cocchi also said that Asclepiades, did not dread the dangers of alienship, feeling himself to be of an innocent nature and without ambition (Cocchi, 1748 in Green). Raynaud said of Asclepiades that, “while not quite in any civil law way, he was at least considered to be a Roman by way of custom and friendship” (Raynaud, 1862).

Following an archaeological excavation in the early eighteenth century, a marble “herm” (a head and torso statue piece), was found buried within the ancient walls of Rome near the gate of the Porta Carpena situated on the Via Appia. The marble square base of this herm was engraved with the name *Asclepiades* in Greek letter print: ΑΣΚΛΗΠΙΙΑΔΗΣ (Raynaud, 1862). The herm depicts Asclepiades bare headed, with his hair short and without a beard. He is not wearing a Roman toga. The noted Italian philologist and classicist Biagio Garafalo (1677-1762) subsequently ascribed this herm to be that of Asclepiades of Bithynia (Garafalo, 1712). This is the only known bust of Asclepiades of Bithynia. It is now located among other Epicurean philosophers in the Room of the Capitoline Museum in Rome, known as the Campidoglio.

It is believed by most scholars that Asclepiades remained in Rome for the remainder of his life. Flemming has postulated that Asclepiades, after he became established as a physician in Rome, probably moved on from an initial phase of frenetic self-promotion and the chasing of elite patients and patrons to a period of intellectual consolidation and medical system building (Flemming, 2012).

3.4.4 The Death of Asclepiades

The precise date of Asclepiades’ death remains somewhat uncertain, with estimates ranging from c91 BC to 40 BC. It appears that Asclepiades did not suffer from a significant illness during his long life. In his *Historia Naturalis*, Pliny writes that Asclepiades had made a bet with the mythical star Fortune, where Asclepiades bragged that if he ever fell ill, no one would believe him he was a doctor (Pliny N.H. 7.37). If

we are to believe Pliny, Asclepiades died having fallen down some stairs (Pliny, N.H.7). Pliny's dating of Asclepiades death to the time of Pompey (Pliny, NH, 26:3,12) is now considered to be incorrect. Most scholars agree and the most likely time of Asclepiades' death was around 40 BC. Arguments about the date of Asclepiades death must begin and end with the well-known passage of Cicero's, *De Oratore*, which refers to the dramatic date of 91 BC. In this passage, Cicero refers to the great orator, Lucius Crassus speaking of "having enjoyed his (Asclepiades') services as both a friend and doctor in the past when Asclepiades used to defeat his medical competitors by his eloquence, and above all by his expertise" (De Oratore, 1.14.62; Rawson, 1982). Rawson argues, that as Crassus mentions Asclepiades in the past tense, then he must have been dead before 91 BC. However, Yapijakis and Flemming emphasize the rather flimsy nature of Rawson's influence and argue that Asclepiades is likely to have lived on into the 80's BC (Rawson, 1982; Yapijakis, 2009; Flemming, 2012).

For the purpose of this thesis, it is assumed that Asclepiades lived from approximately 124 BC to approximately 40 BC, with due note of the uncertainty that inevitably surrounds precise dates from this era in history.

Chapter 4: Asclepiades' Thought, Work, and Context

This thesis chapter explores the themes of “molecules”, “pores”, and “voids” in Asclepiades’ thought processes (Section 4.1), as well as his views on treatments for acute and chronic diseases (Section 4.2), and especially his approach to mental illness (which is a particular focus of this thesis) (Section 4.3). The various medical schools (sects) present at the time of Asclepiades (Section 4.4) are outlined, as are the main supporters and detractors of Asclepiades (Section 4.5).

4.1 “Corpuscula”, “Pores”, and “Voids” in Asclepiades’ Thoughts

When Asclepiades arrived in Rome, he was promulgating a new medical practice system that boldly rejected the Hippocratic doctrine of the four humors (black bile, yellow bile, blood and phlegm), as well as its benevolent nature axiom. Influenced by Epicurean philosophy, Asclepiades adhered to the Atomic Theory of chance and evolution insisting that, “nature does not look after living organisms and is not endowed with specific and mysterious healing facilities” (Edelstein, 1967; Yapijakis, 2009). Asclepiades also challenged the long-established Hippocratic concept of the so-called “critical days” of acute diseases (Yapijakis, 2009). Unlike his Greek predecessors Herophilos and Erasistratus, Asclepiades held that a fully-fledged theory of matter was necessary for the practice of medicine, devoting a treatise to expounding his theory, “On Elements” (Leith, 2020; Galen: *De elementis ex Hippocrate* 9.25-26) of which only fragments remain (Leith, 2020).

4.1.1 *Asclepiades’ Pathophysiological Corpuscular Theory*

When Asclepiades first arrived in Rome, he was positing an innovative systematic medical theory which drew extensively on Epicurean atomism. According to his doctrine, Asclepiades was saying that the human body, as well as everything else in the universe, is made up of tiny imperceptible seamless particles which were in perpetual motion bouncing around in a void space.

There was a myriad of different terms used in ancient literature to describe such particles. Yapijakis has said that Epicurus as well as other Greek Epicureans like Asclepiades, were using different terms when describing such particles. Such terms included: ἄτομα; ἄτομα τῶν σωμάτων (=atoms) as well as ὄγκοι/ συγκρίσεις (=composite bodies made of atoms, i.e. molecules). Roman Epicureans, such as the poet Lucretius used corpuscula (=small bodies), or occasionally minima (=minimal bodies). The Roman Methodic physicians referred to Asclepiadean onkoi as molecules or corpuscula. Yapijakis further added that the term meree (μέρη) could be used for the fragmented (fragmenta) parts of onkoi (Yapijakis, 2024). In view of the above, the term onkoi will be used by this author throughout the course of this thesis.

Asclepiades was saying that the onkoi were moving in perpetual motion, bouncing around forever in a void space, without any providential intelligence at work in the universe to guide them. Just like Epicurean atoms, these onkoi would be of different sizes and shapes, but were devoid of any secondary qualities such as colour, smell or taste. Leith has said that such secondary qualities would only arise when the onkoi combined and reformed into larger masses (Leith, 2023). While similar in many ways to the earlier atomic theories of Leucippus, Democritus and Epicurus, Asclepiades' onkoi were not atoms in the strict sense of the word as had been described earlier, but rather were molecules (composite bodies made up of atoms).

The significant difference between the indivisible atoms of Epicurus and the onkoi being postulated by Asclepiades, was that the onkoi were unique in that they were capable of splitting into innumerable smaller fragments (Toulman and Goodfield, 1962; Yapijakis, 2009; Leith, 2012). Yapijakis has suggested that these broken off portions of the onkoi should be referred to as “fragmenta, or meree” (Yapijakis, 2024). It was an intrinsic part of Asclepiadean theory that the onkoi would move about in the body passing through void gaps or pores that existed throughout the entire body, with health being maintained by their balanced flow, while disease arose principally from blockages of the onkoi in different parts of the body (Asmis, 1993; Yapijakis, 2009; Leith, 2009 and 2012). The fragmenta (meree), because of their smaller size and different shapes had the additional capacity to pass through smaller pores and channels

than the larger onkoi, thus accounting for different diseases occurring at different sites in the body.

4.1.2 *Asclepiades and Epicurus*

Three hundred years after Epicurus and during Asclepiades' lifetime, the Roman poet and philosopher Lucretius (c99 BC-c55 BC), recorded in his famous philosophical poem *De Rerum Natura* many of the tenets of the atomic theories that had been espoused by Epicurus and Asclepiades (Bailey, 1921). Vallance argued that because Asclepiades' onkoi are so fundamentally different to Epicurean atoms (owing to their frangibility), that any influence from Epicurean physics should be rejected, and like Rawson he argues for a closer relationship to Erasistratus rather than to Epicurus (Vallance, 1993). However, Casadei, argued that Vallance tended to suppress several fundamental elements of Asclepiades' doctrine (Casadei, 1997).

Adding to the discussion, Polito had put forward the philosophical view that Asclepiades cannot be regarded as an Epicurean physician because he felt that there were distinct non-Epicurean elements in Asclepiades' theory system, such as radical determinism and his denial of a localized ruling part of the soul (Polito, 2006). However, several other scholars have given more balanced opinions on this contentious issue (Lonie, 1964 and 1965; Furley, 1967; Yapijakis 2009). Stückelberger traces a direct line from Democritus through Erasistratus and then on to Asclepiades and subsequently to Lucretius (Stückelberger, 1972).

In a recent important publication, Leith addresses the somewhat complex nature of the relationship between Asclepiades and Epicurus and concludes "that it is evident from detailed and precise doctrinal parallels, that Epicurus was Asclepiades' main intellectual inspiration in his epistemology and in his psychology, and that his scientific method was firmly grounded in Epicureanism". He goes on to say that "whether this was explicitly acknowledged by him (Asclepiades) remains rather unclear, but whatever the case, Asclepiades offers a rich detailed case study in the wider impact and powerful influence that Epicurean science had in the late Hellenistic and early Roman periods" (Leith, 2023). It is fascinating to note that not only was Epicurus thinking along subatomic particle lines (Yapijakis, 2022), but so was Asclepiades, as his meree

could be viewed as similar in some ways to entities described centuries later by modern physicists, where subatomic particles known as quarks and neutrinos exist within the neutrons and protons in the modern concept of the atomic nucleus (Close, 2004). Nevertheless, it is more probable that Asclepiades' meree (or fragmenta), were parts of broken onkoi (Yapijakis, 2009 and 2017).

Asclepiades pathophysiological ("corpuscular") theory of matter was partly derived from the earlier atomic theories of Leucippus and Democritus, as well as being heavily influenced by Epicurean philosophy (Haller, 1776; Gumpert, 1794; Blumenbach, 1786; Zeller, 1909; DeWitt, 1932; Singer and Underwood, 1962; Leith, 2009, 2012 and 2023; Yapijakis, 2009 and 2017). As a result, the issue of its originality merits attention.

4.1.3 The Originality of Asclepiades' Theory

The issue of whether Asclepiades' theory of matter was entirely unique to him or was largely a replication of the earlier atomic theories of matter that had been put forward by the philosophers Heraclides of Pontus and Epicurus, has been the subject of considerable scholarly debate over the years with sharply divided views. Heidel in 1909 argued that Asclepiades' onkoi possessed secondary sensible qualities, such as colour, taste and smell (Heidel, 1909). More recently, Lonie took the view that Asclepiades' physical theory was essentially the same as that of Heraclides of Pontus and in some ways also like Plato's mathematical triangular model (Lonie, 1964 and 1965). Gottschalk subsequently took a similar view to Lonie saying that Asclepiades' theory in many ways replicated Heraclides earlier theory (Gottschalk, 1980).

Heraclides was born in about 387 BC in Heraclea Pontica, now Karadeniz Erêgli in modern day Turkey. All his writings are lost, except for some fragments. Gottschalk notes that Heraclides was a student of Plato and had been a distinguished member of the Academy. According to Vallance, Galen's commentary on Plato's *Timeaus* said that many members of the Academy, which probably included Heraclides, were interested in developing the physical mathematical doctrines of Plato (Vallance, 1990).

However, it must be noted that little is known of Heraclides' own theoretical corpuscular theory (Gottschalk, 1980).

Elisabeth Rawson refers to some earlier physicians who had mentioned theoretical pores and blockages, but not as consistently as Asclepiades. Rawson goes on to say "that in the context of a corpuscular theory, she suggested that it was Erasistratus, as opposed to Heraclides and Epicurus, who was perhaps Asclepiades' closest intellectual predecessor (Rawson, 1985).

Yapijakis mentions a number of reasons that support beyond any reasonable doubt the thesis that Asclepiades was influenced by Epicurean philosophy and not by the Platonic philosopher Heraclides of Pontus:

1. Asclepiades accepted the notion that the soul was made of atoms and *onkoi* like any other part of the body and therefore dissolved after death. This was an Epicurean and not a Platonic doctrine.

2. The consideration of a patient's pleasure is an integral component in Asclepiades' medical practice. Pleasure for Epicurus was the primary good and the most familiar to human nature, while for Plato it was the last of the minor goods.

3. The vast majority of Greek physicians (including Hippocrates, Galen, Herophilus and the Empiricists) admitted that divine dream-healings and mantic dreams were real and effective. The Methodic physicians were the only ones that apparently did not believe in divine dreams and they never mention them. This exception parallels the fact that almost all Greek philosophers believed in mantic dreams except Epicurus.

4. Heraclides of Pontus indeed proposed a corpuscular theory using the term *ongoi*, but his works were also loaded with supernatural narrations and imaginary miracles, and he was famous for his egocentric attitude and vain personality. Heraclides does not fit at all the personality model for a science-oriented, decent and compassionate physician like Asclepiades. On the contrary, the Bithynian shares many qualities of Epicurus, who was famous for his naturalistic thinking, modesty, kindness and friendliness.

5. Despite the claim of some modern authors that "there is no evidence for an 'Epicurean' school of medicine", there is mounting archeological evidence for the

existence of Epicurean physicians, e.g. in Rhodiapolis (Asia Minor), in Rimini (Italy), the medical text of the Roman era ‘Precepts’ that combines ideas of Epicurus and Asclepiades (Yapijakis, 2009).

This theory of the onkoi and their fragility had direct implications for Asclepiades views on medical treatment, which are now considered next.

4.2 Asclepiades on Treatments

4.2.1 *Asclepiades’ Theory of Health and Disease*

According to the physiological and pathological theory posited by Asclepiades, good health is maintained by the free and balanced motion of the onkoi through pores that lie within a void space, while disease is primarily the consequence of the blockage or impaction of the onkoi in a particular part of the body, with different diseases resulting from blockages in different parts of the body. Leith said that this localization of pathological phenomena was absolutely fundamental to Asclepiades’ approach to diagnosis and treatment (Leith, 2020).

Such an imbalance between onkoi and pores, could result from alterations in form, shape and size of the onkoi, as well as constrictions (blockages) or dilation of the pores within the body (Gumpert, 1794; Green [Cocchi] 1995; Rawson, 1985; Vallance, 1993; Yapijakis, 2009; Leith, 2009, 2012, 2020 and 2023). Leith added that as a significant corollary to Asclepiades’ particle physics theory is that there are absolutely no impermeable structures within the human body (Leith, 2020). This specific localization of pathological phenomena was fundamental to Asclepiades’ approach to diagnosis and treatment” (Leith, 2023).

Asclepiades held that the state of the pores was crucial to an understanding of how various diseases presented clinically. For example, if the pores in any part of the body were too narrow or too wide, this could affect the movement of the onkoi through the pores, thus contributing to the course of the disease (Leith, 2009). Yapijakis has expressed Asclepiades’ theory of human disease as being caused by alteration in form,

position of the free flow of individual molecules through the porous system. Thus, Asclepiades was introducing the concept of what is referred to today as “molecular stereopathology” (Yapijakis, 2009).

Asclepiades was also positing that the vital heat of the human body occurred because of friction between the constantly moving onkoi, and not as the result of any “vital fire”, as had been postulated earlier by Empedocles (Toulmin and Goodfield, 1962).

4.2.2 Asclepiades’ Therapeutic Remedies

Vivian Nutton has said that what gained Asclepiades his medical reputation in Rome was less to do with his theories and more to do with his therapies (Nutton, 2024). Asclepiades’ therapeutic remedies were essentially mechanistic, aimed primarily at restoring harmony between the motion of the onkoi and the size of the apertures of the pores. As a physician, Asclepiades was distinguished by two personal qualities, compassion and common sense. He generally avoided the drastic therapeutic remedies fashionable at the time amongst his contemporaries and immediate predecessors (Rawson, 1985). At the same time, he courageously denounced the Hippocratic approach to the treatment of chronic and incurable illnesses. Gumpert said that Asclepiades regarded the long-standing Hippocratic approach to incurable diseases, which was practiced by his predecessors, as “a training for death” (Gumpert, 1794). Asclepiades always tried to treat patients with incurable diseases in a manner to make their life as pleasant as possible. In this context, Yapijakis noted that “if belief in afterlife is denied, it follows that life and health of body and soul becomes the most precious possessions of mortal man. Asclepiades thought that the physician had to assist people to achieve physical and mental health as well as to subsequently let them hope that they would keep this pleasant state of life for long” (Yapijakis, 2009).

Differing from the existing practices of the followers of Hippocrates, it was only in extreme cases that Asclepiades recommended and indulged in therapeutic activities

such as bloodletting, enemas, and purging procedures, all of which were the most used therapies of that era (Lonie, 1965; Yapijakis, 2009; Santacroce et al., 2017). As a result, Asclepiades' approach to the practice of medicine was diametrically opposed to that of his Greek predecessor Archagathus, who practiced in Rome around a century before Asclepiades arrival there. Asclepiades' personality, careful manners, and gentleness with his patients helped him considerably in overcoming the Roman population's general misgivings about Greek physicians (Yapijakis, 2009).

In treating acute medical conditions, Celsus refers to Asclepiades advocating that the doctor must treat his patients "safely, swiftly and pleasantly" (*Asclepiades officium ease medici dicit, utu to ut celeriter, at Jocund*), to have the best possibility of a cure (Cels. Medd.3.4.1). Whereas in chronic incurable medical conditions, Asclepiades argued that the best way to deal with incurable or chronic medical conditions was to provide comfort for the patient in a carrying, sympathetic and humane manner (Cocchi, 1758; Gumpert, 1794; Raynaud, 1862; Yapijakis, 2009).

Asclepiades held that many of the ancient herbal remedies were bad for the stomach. He said that such drugs should not be administered to patients with fevers. He suggested that it was preferable to give such patients carefully regulated amounts of food and wine. He also said that it was wise for the physician to have a list of various proven compositions, not for each individual element, but for perhaps two or three, prepared and tested in advance. (Leith, 2021).

To restore and maintain a patient in good health, Asclepiades was advising a therapeutic approach that was based on five main principles:

1. *Diet*: Asclepiades recommended the regular intake of a healthy diet of food as well as fresh water for adequate hydration. In some instances, he suggested imbibing of moderate amounts of usually diluted wine (Rawson, 1982; Yapijakis, 2009);
2. *Exercise*: This was recommended for patients who were unable to exercise independently. Such activities included gentle exercises on swinging/ swaying couches which he had specifically designed ("pensilia"). These could also be modified for hydrotherapeutic techniques in so called swinging hanging baths (known as "balnea pensilia") (Benedum, 1967);

3. *Massage*: Asclepiades placed great emphasis on gentle massages in well-lit rooms, located in congenial surroundings with ample fresh air;
4. *Bathing*: He also recommended regular bathing in cold or warm water, depending on the specific clinical condition, which would be followed by passive supervised gentle exercises;
5. *Music*: Asclepiades was also a great supporter of selected forms of music for certain individual mental conditions, such as depression.

While critical of Hippocratic views on the causation of diseases, Asclepiades did use the Corpus as a storehouse of practical information, rather than for its theories. He also rejected the Hippocratic doctrine of “critical days,” although probably not the notion of “crises” (Leith, 2021).

Asclepiades general therapeutic approach was very well received by his patients, especially by his wealthy ones (Pliny, Hist. Nat. 23,19,31-32; Caelius Aurelianus, Acute Diseases 2,58; cf as “wine givers”). Throughout all of his medical therapies, Asclepiades emphasized that the physician should pay as much attention to the whole process of convalescence for the recovering patient. In this regard, Asclepiades appears to have been a very reasonable and prudent doctor. Nutton has said that he was “way ahead of his time” in his therapeutic approaches (Nutton, 2005).

4.2.3 *Asclepiades and Medicinal Drugs*

Asclepiades was not opposed to the use of drugs, as some scholars have suggested (Scribonius Largus, Drug Recipes, pref. 3-4; Celsus, On Medicines 3, 4,2). He was one of the first of the ancient physicians to recognize the dangers of the indiscriminate use of drugs and herbs. He wisely restricted the use of particular drugs to specific conditions. Indeed, owing to his detailed knowledge of medical herbs, Asclepiades was frequently referred to in Rome as “pharmacion” (Scarborough, 1975; Flannery, 2001; Yapijakis, 2009; Francia and Stobart, 2014).

As a further testament to his knowledge of drugs and herbal medications, King Mithridates of Pontus (135 BC-63 BC) invited Asclepiades to leave Rome and join his

court in Pontus as the King's senior physician. The King had an obsessive interest in pharmacology, especially poisons. Asclepiades declined the King's invitation but did send him several copies of his precepts (Pliny. H.N. XXV.3 and VII.37). All of this strongly suggests that Asclepiades not only had a deep knowledge of plant herbs and drugs in general but also showed personal integrity in spurning the immense riches of the court of King Mithridates. The king was an enemy of Rome, so Asclepiades' decision not to go to the King's court, despite the promise of enormous riches, was very well received by the Roman ruling classes.

Asclepiades was also very wary of using certain powerful drugs which were popular with many other doctors at the time, such as Hellebore. He also restricted the use of other commonly used remedies, such as oxymel to cure snakebites. He did use clysters to purge the bowel in certain situations, though not as frequently or as violently as most his predecessors (Nutton, 2024) Leith has pointed out that Asclepiades did not rule out the use of emetics when he felt it was necessary to do so and in cases of dropsy he would consider the use of venesection and tapping (Leith, 2021).

4.3 Asclepiades and Mental Illness

Asclepiades' approach to managing mental illnesses was notably humane and reasoned, contrasting with many methods of the harsher methods of treatment common at that time. His emphasis on a more compassionate and patient-centered approach is now seen as being ahead of his time and resonates with contemporary views on the treatment of mental health (Yapijakis, 2009). Asclepiades was a strong advocate for the mentally ill. He made extensive contributions to understanding mental conditions. For example, he clearly understood the differences between hallucinations and delusions, and his theory of disease mechanisms made it obvious to him that mental disease occurred as the result of impaired *onkoi* in the brain area (Thumiger and Singer, 2018) Asclepiades' therapeutic approach to patients with mental illnesses was essentially similar to his treatment approach to patients with physical illnesses. He would treat mental disorders in a very humane manner. At that time in Rome, it was common practice for people who were considered to be insane to be locked up in dark

confined places which were essentially dungeons (King, 2006). Asclepiades believed that this inhumane approach would only further misalign the brain onkoi. He advocated that patients with mental illness should be released from these places of confinement, which would have been terrifying for such patients, so that they could be properly treated in a manner as he was suggesting. His primary therapeutic aim was to provide a comfortable setting for those affected with mental disorders so that his natural recommended regimens of therapy could be provided safely and sympathetically, thus allowing harmony between the patient's onkoi and the pores in their brain. This approach was in stark contrast to the barbaric treatment of mental illnesses that existed in Rome at that time (Gertz, 1994; Harris, 2013). Asclepiades' treatments were surprisingly modern in their approach to the management of mental illnesses. As already mentioned, he also showed a remarkable awareness to the nuances of behavior by distinguishing the difference between delusions and hallucinations, which at that time most Greek and Roman physicians' thought were identical. He was also aware of emotional disturbances, which he referred to as "passions of the sensations". Asclepiades is considered by many academic physicians today as being the pioneer of the humane approach that is undertaken in modern psychotherapy and psychiatry (Yapijakis, 2009).

4.3.1 History of the Ancient Understanding of Mental Illness

Millon writes that "the origins of the interest in the workings of the human mind were in their earliest form connected to the study of astronomy and to the spiritual unknowns" (Millon, 2004). Early humans and ancient civilizations associated mental illness with magical spells, sorcery, and metaphysical or divine evil spirits that lay within the human body. They attributed unusual human behavior which they did not understand to either the malignant influences of other humans (by magic) or divine interventions (by gods).

By whatever manner these humans became possessed, the presence of such spirits was often viewed by the ancients as a punishment for not obeying the teachings of priests or gods.

This conception of demonological mysticism allowed charlatanism to flourish in these communities. Wizards, sorcerers, and priests (shamans) became very powerful by capitalizing on the fears of the populace, offering them healing methods aimed at “purifying” the bodies of the mentally distressed (Tzeferakos and Douzenis, 2014). Fears that these evil spirits might spread to afflict others frequently led to cruel and barbaric methods of so-called treatment. People with mental illnesses were often incarcerated in poorly lit, damp dungeons. They were commonly mechanically restrained in chains and deprived of food and water. When such treatments failed and it was felt that the gods had not been appeased, it was not unusual that these people were put to death (Longrigg, 2013).

Surgical interventions in treating mental illnesses were also relatively common. The most common method involved the boring of a hole into the vault of the skull using a technique known as trephining or trepanning. This was performed in the hope that it would facilitate the escape of the evil spirits through the hole in the skull and allowing them to pass into the atmosphere where it was felt that these spirits would eventually die (Brothwell, 1977; Mariani-Constantini, 2000; Fernando et al, 2003; Millon, 2004; Tullo, 2010).

Attempt to treat mental illness date back to Egyptian times. There are two papyri dating back to the sixth century BC. The Edwin Smith papyrus and the Ebers papyrus include, very likely for the first time, references to the brain as the site of mental functions (Hartsock and Halverson, 2023).

However, over time Greek philosophers started to question these traditional methods of treatment and seek a sounder basis to assist such people. A fundamental shift began to take place, not merely in describing different types of mental disorder, but in providing a sounder basis for thinking about ways to alter these aberrant behaviors. To treat mental disorders these philosophical thinkers began to recognize how and why mental disorders were expressed in the natural world. Only then could they successfully deal therapeutically with the tangible symptoms of everyday mental disorders. A more concretely orientated perspective began to emerge. This transition was led by imaginative thinkers in the fifth and sixth centuries BC (Millon, 2004).

In ancient medicine, known mainly through the vast corpus of Greek and Latin medical writings, there appears to have been no established term, or neat category, corresponding to “mental illness” as it is understood today (Ahonen, 2019). Words denoting “madness” and “derangement”, such as “mania” in Greek or “insania” and “furor” in Latin, could be also used for excessive behaviors and various mental states, as well as what is now known as mental illness (Padel, 1995). Many physical diseases and illnesses are described in ancient texts. References to conditions affecting mood, judgement, and memory are listed, with periodic references to the conditions that affect the mind and the soul. Plato and Aristotle wrote about the importance of fantasies and dreams, thus anticipating (to some extent) the fields of psychoanalytical thought and cognitive science, and later developments in psychiatry.

This lack of distinction between mental and physical illness in ancient texts meant that symptoms such as headache and paralysis were often described in the overall context of the clinical condition of the patient and not considered to be a distinct medical category. Among the exceptions to this rule, Hippocrates in his “On the Sacred Disease”, does described madness as a wet condition of the brain but this was the exception rather than the rule during this period (Jouanna, 1999).

Around the sixth century BC, philosophers started to think about attributing inner thoughts and feelings to possible natural forces that lay within people themselves, which might also shape a wide range of psychological processes (Alexander and Selesnick, 1966). This movement incorporated an attempt to explain diseases of the mind in physical terms, was an attempt to find a psychological explanation for mental disturbances (Tzeferakos and Douzenis, 2014).

From Democritus and Socrates onwards, numerous philosophers began to profess themselves to be “doctors of the soul” who attended to the ills of the soul, while physicians took care of the “ills of the body” (Ahonen, 2019).

There were three major Greek philosophical schools at that time: the Stoics, the Epicureans, and the Sceptics. Each of these schools had their own individual views on the therapeutic approach to mental illness, as part of this broader shift. In general, their approaches were mostly cognitive, i.e., concerned with thinking.

4.3.2 Defining Mental Illness in the Ancient World

In ancient Greco-Roman times, a wide variety of words were used to denote mental illness and people who were mentally ill. In Latin, common terms include mania, insania, fanaticus, non-compos mentis, demons, ideotus, furious, or furor. According to Gazmuri, Cicero “established the use of two different terms to distinguish between the moral or philosophical madness (of the soul), which he called insania (unsoundness of mind), and medical derangement which he called furor [frenzy]” (Gazmuri, 2006). This distinction between furor and insania is based on the Stoic doctrine which proposes reason as the main guideline of life, based on Socratic teaching (Taldone, 1993).

For the Stoics, “madness was a disease of the soul, characterized by the primacy of passions over reason” (Gazmuri, 2006). The Stoic approach found a favorable reception among the Romans probably because the archaic Italic tradition substantially agreed with the volitive-emotional approach of the Stoics (Gazmuri, 2006).

In the second century AD, Greek philosopher Celsus proposed that there were three main types of mental illness: firstly, an acute affliction associated with fever (e.g., phrenitis); secondly, a chronic mental illness without fever (e.g., melancholia), and thirdly, a particular type of chronic mental illness that was generally characterized by mental confusion and hallucinations, although the term schizophrenia was not used at that time (Jackson, 1986). In the Hippocratic Corpus, the concept of mania (madness) was not precisely determined. In the Hippocratic Schools teachings, madness was defined by most as a loss of mind and a change in customs and habits (Roccatagliata, 1986).

Up until the sixth century BC, ancient western cultures attributed mental illness to a variety of gods who could both cause and cure madness (mania). In general, any aberrant behavior was believed to be caused by the wrath of a god or a demonic force which resulted in the mental condition. In his *Phaedrus*, Plato distinguished between medical madness and divine madness. He states that there are two kinds of mania, one which involves mental harm with a bodily cause of origin, and another which was

described as a divine madness, which could be of three different kinds: prophetic, erotic, and poetic sub-types (Gazmuri, 2006).

In Rome, mental disease was given a solely sacred interpretation in 289 BC with the foundation of the Temple of Asclepius (Edelstein, 1967). Romans used to turn to the college of the Augurs and the Sibylline books to resolve their medical and psychiatric problems (Roccatagliata, 1996).

However, over time things started to change. Gazmuri writes that in the sixth century BC, the philosophers of Ionia elaborated a biological model of mental disease on a purely materialistic approach, which served to introduce psychiatry into the realm of the science of nature, separating it from the sacred world and from philosophical speculation (Roccatagliata, 1996; Pigeaud, 1987; Gazmuri, 2006).

Hippocrates had previously proposed that mental diseases were due to toxic effects produced in the brain and its psychic pneuma, which had occurred because of an imbalance in the bodily humors (Gazmuri, 2006).

4.3.3 *Phrenitis: “An Affliction of the Mind”*

The term “phrenitis” or “aphrosyne” (“lack of phronesis”) was first employed in ancient Greece medical thought by Hippocrates and his followers. They were saying that it was an “affliction of the mind” which was accompanied by an acute fever with resultant delirium. The presumed location of the condition within the body was never anatomically or conceptually well determined. The word phrenitis itself is derived from the Greek for diaphragm, which suggests that the condition might have been regarded as being associated with the heart. In keeping with Hippocratic thinking, phrenitis was also thought to be due to an excess of yellow bile within the humoral system in the body (Jackson, 1986).

The diagnosis of phrenitis was a descriptive one which suggested an acute inflammation of the mind and body. Hippocrates was the first to attempt a detailed description of the condition and, in the Hippocratic Corpus, there is mention of approximately 37 case studies with the clinical features of phrenitis, although the

Corpus seldom mentions the actual word (Cilliers and Retief, 2009). The clinical features described varied widely, ranging from short-lived headaches with slight fever to more serious states of drowsiness and confusion in patients who would often pluck at their garments or bedding. Patients with the condition might also engage in meaningless conversation and go silent for long periods, alternating with bouts of hyperactivity which would be followed by severe fever, paralysis, coma, and ultimately death (Ahonen, 2019). Certain authors claimed that Hippocrates never prescribed any treatment for phrenitis, but Simon (1978) and von Staden (1989) refer to Hippocrates suggesting a therapeutic regimen for acute delirium and hallucinations associated with a fever, involving purgatives, sweet wine, and a mixture of soup, honey, and vinegar (Simon, 1978; von Staden, 1989).

The term phrenitis was mentioned by later Greek physicians such as Herophilus, his pupil Democritus, Asclepiades, and Soranus (98 AD-138 AD), whose work was recorded in the fifth century AD by Caelius Aurelianus (Drabkin, 1950). The concept of phrenitis persisted up to the nineteenth century, when it was replaced by “delirium”, a term that is currently accepted as being a serious disturbance in mental abilities that results in confused thinking and reduced awareness of the environment. Other contemporary terms for conditions likely linked with phrenitis included “meningitis” and “encephalitis” (Frederiks, 2011).

4.3.4 *Asclepiades and Phrenitis*

In the first book of his *De Morbis Acutis* Caelius Aurelianus gives, what he implies is a Asclepiadean definition of phrenitis, as being stasis, obstruction or blockage of corpuscles in the cerebral membranes which occur frequently and without any sympathetic affection, but with mental alienation and fever (Drabkin, 1950).

Caelius argued that Asclepiades’ theory on the etiology of phrenitis was that the cerebral membranes, for whatever reason, became heated and the onkoi moved

towards the meninges and brain. Subsequent crowding of the onkoi resulted in phrenitis. Asclepiades went on to say that the many of these onkoi were repelled because the meninges were unable to accommodate them, and these repelled conglomerates of onkoi then moved to other parts of the body, such as to the intestines, resulting in “loosening of the belly” (Drabkin, 1950).

For more of Asclepiades’ views on phrenitis, it is necessary to look to Drabkin’s translation into English of Caelius’s Latin translation of Soranus’ *De Morbis Acutis et Chronicis* (“On Acute Diseases and on Chronic Diseases”), which was originally written in Greek. Caelius’ first book, *De Morbis Acutis*, is the best documented account of phrenitis in the ancient literature. As a Methodist physician, Soranus was critical of what he felt were omissions by Asclepiades of what Soranus believed were important physical symptoms of the condition. According to Soranus, Asclepiades erred in trying to explain the cause of phrenitis, rather than focusing on the signs and symptoms of the disease. This criticism of Asclepiades by Soranus is not surprising as all that a Methodist physician needed to know where the visible signs of a disease, rather than its causes (Vallance, 1990). Galen, in his treatise, “On Medical Experience”, gave a different account of Asclepiades’ phrenitis and just seemed more interested in attacking Asclepiades’ corpuscular theory, rather than the clinical details. Galen did not mention any of the signs of phrenitis as had been ascribed to Asclepiades in Caelius’s text.

The two sources which best explore Asclepiades’ recommended treatment of phrenitis are Caelius Aurelianus and Antonio Cocchi. Asclepiades’ guiding principle in treating any acute medical condition such as phrenitis was that the physician had to act “safely, swiftly and pleasantly” (*cito, tutu, jucunde*). Patients should be placed in bright, aerated, well-lit rooms, and never in dark surroundings. Adequate hydration with tepid water was recommended twice daily. As diet was a very important component of treatment, Asclepiades suggested providing easily digestible foods, in small amounts, three times daily. Pliny said that Asclepiades condemned the use of enemas in the treatment of phrenitis, but this was not the case. In fact, Asclepiades advised that enemas could be considered in certain presentations of the disease depending on the individual’s particular clinical situation. Asclepiades did oppose purging the phrenetic patient, in keeping with his corpuscular theory. He was opposed

to bloodletting (venesection) in cases of phrenitis, on the basis that the onkoi involved in phrenitis were very small, but plentiful, and venesection would lead to a greater concentration of these conglomerates of small onkoi with increased obstruction within the interstices of the brain membranes and in the brain itself. This, he argued, would lead to a deterioration in the condition.

In terms of the timing of treatment, Asclepiades believed that there were no “critical days” of diseases, meaning that illnesses did not end at a definitive time. He suggested that physicians should manage phrenitis in a carefully staged manner. On the first day, he recommended giving little food, but asking the patient to take plenty of cold drinks. He suggested offering a choice of drinks to the patient, but no wine at this point. On the second day, if the fever was persisting, he suggested that there should be no solid food intake and fluid intake should be restricted. It was appropriate to provide moderate amounts of cold water twice daily. The patient should be watched closely during this second night. By the third day, he said that most patients would have started to show clinical improvement. As their temperature started to fall, he encouraged soft solid foods. As their condition continued to improve, they could then take more solid food. By the seventh day, the patient should be eating bread and fish, and taking small quantities of wine, initially diluted (Cocchi, 1758; Green, 1955).

4.3.5 Asclepiades and Melancholia

The word melancholia, or melancholy, is derived from the Greek “melaena chole”, meaning black bile (Bell, 2014). According to Hippocrates and his followers, melancholia was caused by an excess of black bile, which would then thicken and cause the condition (Stanley, 1983; Jackson, 1986; Berrios, 1996). In his *Aphorisms*, Hippocrates characterized melancholia as an affected mental disorder in which the clinical features of fear, sadness and despondency persisted for an extended period (Jones, 1923). Hippocrates mentioned that melancholia could be associated with epilepsy and on occasion hallucinations and delusions. Melancholia is only mentioned sporadically in the Hippocratic Corpus (Jackson, 1986).

This relative neglect of melancholia is not surprising during this period of ancient history as there was no established term for mental illness” (Ahonen, 2019). Aristotle, interestingly, referred to melancholy as being a characteristic of gifted people. He theorized that there were two types of black bile, “dry” and “wet”, and that an excess of dry black bile caused depression, whereas an excess of wet black bile caused mania (Cilliers and Retief, 2009). Despite these differing interpretations of the nature and causes of melancholia and mania in ancient times, it is clear that the Hippocratic clinical description of melancholia shows significant overlap with contemporary descriptions of depressive conditions as outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 2013).

In his monumental eight-book treatise *De Medicina*, Celsus wrote favorably about Asclepiades and his treatments for melancholia. While Celsus was a distinguished Roman encyclopedist, it is unclear if he was a physician. Nonetheless, he says of Asclepiades that by his concentration on dietetics, the healthy regime, as opposed to pharmacology or surgery, Asclepiades had introduced an entirely new epoch to Roman medicine (Mudry, 1993). Celsus records Asclepiades as saying that sufferers of melancholia respond differently to light or dark rooms with some preferring to be kept in dark rooms while others prefer well-lit spaces. Asclepiades argued that treatment for melancholia depended on the individual patient’s needs, and that the physician should be sensitive to their individual needs. Asclepiades added: *Neutrum autem perpetuum est: alium enim lux, alium tenebrae magis turbent*; i.e. “Neither way is always right: light upsets some and darkness upsets others”.

When Asclepiades first arrived in Rome, it was common for the local physicians to administer a wide variety of herbal remedies in the treatment of mental afflictions, including melancholia. Such treatments included shaving the patient’s head and then rubbing it with water infused with verbena (a herb). Rose oil could also be poured over the head and into the nostrils. Some patients were advised to inhale rue (a herb) with bitter-sweet solanum (a plant traditionally used to treat tuberculosis). Muralis (another plant) mixed with vinegar could also be rubbed into the head to alleviate delusions and sadness. Another form of treatment was a scalp rub remedy using saffron mixed with orris (root). Concoctions of poppy or Hyoscyamus mixed with water were also

recommended for “composing the mind”, while other doctors recommended smearing the forehead with cardamomum balsam or sycamine tears (*amomum vel sycamine lacramam fronti inducunt*).

Not all physicians agreed with these herbal remedies and Celsus records Asclepiades as saying that, in general, herbal remedies for melancholia, “are of no use in the long term”. Asclepiades was recommending an alternative approach to treatment of melancholia based in large part, but not exclusively, on his five main principles of therapy (as outlined above), but adapted them for the condition of melancholia:

1. *Diet*: Asclepiades recommended regular intake of healthy fresh food and fresh water, and (sometimes) moderate amounts of wine (Rawson, 1982; Yapijakis, 2009). Pliny sarcastically commented that part of the great popularity that Asclepiades enjoyed depended on his prescribing the liberal use of wine to his patients (Pliny.HN.7.37.xxiii.22).
2. *Exercise*: Depending on the individual patient, gentle exercise in the fresh air would often prove highly beneficial. Gently swaying hanging baths, the “*balnea pensilia*” which Asclepiades had designed, were used frequently and these could also be modified for hydrotherapeutic techniques (Benedum, 1967).
3. *Massages*: Asclepiades placed great emphasis on gentle massage in well-lit rooms, in congenial surroundings, with ample fresh air. However, he said that too much hard rubbing could produce lethargy and might not be suitable for severe depression.
4. *Bathing*: Regular bathing in cold or warm water, depending on the specific condition was encouraged. Such bathing was to be followed by passive gentle exercises.
5. *Music*: For patients who suffered from deep anxieties, the physician should try to relieve their fears by explaining how their fears are baseless. Asclepiades used music, cymbals, and certain noises as a therapy for people with mental illness, especially melancholia. He said that hyperexcitable patients responded best to gentle calming music, while those in a somber, depressed state were encouraged to listen to the Phrygian pipes (musical instruments often used for religious purposes). Asclepiades did not recommend the use of a flute in any of his

treatments because he considered this musical instrument to be too energetic and would not produce the desired calming effect (Hordon, 2000; West, 2000; Gonzalez, 2012; McCaffrey, 2015).

One of the other therapies that Asclepiades considered in managing patients with melancholia was to induce sleep using the sound of gently falling water or the feeling of being suspended while lying in a hammock. He recommended trying to revive the patient's interests by reading to them or by playing games with them, regarding storytelling and games as great remedies for depression. The intention was to divert patients away from the fears that were tormenting their minds. Asclepiades said that it was generally better to agree with the patient when engaging with them, rather than contradicting them. In this way, he felt that their mind could be gradually moved from irrational to rational. On occasions, Asclepiades felt that purgatives could help, but he remained opposed to emetics and bloodletting, because they did not accord with his corpuscular theory of disease causation.

4.3.6 Other Mental Conditions in the Ancient World

It is helpful to place Asclepiades' approach to apparent mental illness, especially melancholia, in the context of other approaches to similar mental conditions in the ancient world.

The term "mania" was often used in ancient times as a general term for insanity (madness). Eisenrath et al pointed out that, as formulated in ancient times, mania was being characterized by a depressed temperament, rather than the currently popular concept of it being a hyperactive one (Eisenrath, Lichtmacher, and Haller, 2006). The concept of mania is not precisely determined in the Hippocratic Corpus. In keeping with the views of the pre-Socratic philosophers of the fifth and sixth centuries BC, Hippocrates expressed mental illness in terms of the humoral theory which he felt was attributable to an excess of moisture within the body. However, even Hippocrates did not completely discard the supernatural suggestion, saying that the position of the heavenly bodies could influence a person's mental state. He wrote that mental

conditions occurred mostly in young females and presented as fear and hallucinations. The Methodic physician Soranus later wrote that when it occurred in young men, they would have symptoms such as insomnia, exhaustion, depression as well as hallucinations.

Overall, at this time the medical treatment for both melancholia and mania were aimed towards building up the person's strength and physical constitution as far as possible. Both somatic and psychotherapeutic measures were employed to this end. Later, as a devoted member of the Methodist school, Soranus recommended a calming gentle approach for milder cases, although he reverted to traditional approaches for more serious ones, including restraints for hyperactive patients, bloodletting, and purgatives (Rasen, 1968; Jackson, 1986; Pigeaud, 1987). The calming therapeutic approaches suggested for milder cases were in keeping with those that Asclepiades had previously been advocated, including calm conversation, music, storytelling and even attendance at the theatre.

In his *De Medicina*, Celsus refers to other physicians of the time adopting and advocating more violent physical measures, such as physical restraints, beatings, violent purges, excessive bleedings, and keeping patients in dark, damp dungeons (Celsus, *De Medicina*, 111, 18-19). Asclepiades was of course totally opposed to such measures for the treatment of conditions which we now describe as mental illness.

Other mental illnesses included “hysteria”, which has a long and complex history in psychiatry. Simon noted that many ancient physicians rather bizarrely had held a view that the womb wandered around in the woman's body causing diverse symptoms by pressing on the organs such as the heart, lungs, pharynx and liver. These symptoms were often called “hysterical disturbances”, derived from the Greek word *Hysterios* which was linked in various ways to the womb (Simon, 1978). The “Corpus” describes a clinical picture of loss of voice, stridor, and convulsive spasms. Later, Soranus in his *Gynaecia*, describes “hysterical suffocation” as a condition which results from multiple miscarriages, premature births, and widowhood. He did not, however, consider the uterus to be mobile within the body and regarded those who held such views with contempt (Dysert, 2007). Ever prescient, Soranus speculated that the

subordinate position of women in Greco-Roman society was at least partly responsible for the ancient hysteria syndrome (Simon, 1978).

Catalepsy was also described by various authors and was chiefly associated with young females (Drabkin, 1955). It was characterized by seizures or a trance state, with loss of sensation and muscular rigidity. The occurrence of a seizure along with catalepsy made the individual unconscious and unaware of their situation. Some authors considered catalepsy to be a condition resembling phrenitis and to a certain extent epilepsy but said it should not be confused with lethargy. Catalepsy presented clinically as acute immobilization of the body, staring eyes, loss of voice, muscle spasms, and a tendency to weep (Drabkin, 1955). In some ways, the clinical condition of catalepsy described by Caelius Aurelianus resembles the modern condition of narcolepsy (Drabkin, 1950; Eisenrath and Lichtmacher, 1999).

Epilepsy was widely described in ancient literature. In pre-Hippocratic times it was referred to as a sacred disease. It was thought that the condition was sent by the gods in retribution for some imagined slight on the divine. The afflicted would commonly seek a cure at one of the Asklepiion temples where priests practiced interpretation of dreams, incantations, and a variety of purification agents. The Hippocratic text titled “On the Sacred Disease” is one of the earliest, detailed observations of epilepsy in humans (Adam’s translation, 1999). A consensus of historians believe that the author of this Hippocratic treatise was most likely a younger contemporary of Socrates (Singer and Underwood, 1962).

The author of “On the Sacred Disease” declares that epilepsy is no more sacred than any other disease and has no relationship to the divine. The author argues that the condition is purely of human origin and the brain is the cause of this affliction (Adam’s translation, 1999). Symptoms of epilepsy included shaking uncontrollably, frothing from the mouth, clenching of teeth, and suffocating on their own saliva, along with contractions of the hands and evacuation of the bladder and bowels. The Corpus held that the condition was hereditary in nature and caused by an excess of the humor phlegm in the brain, from where it spread to the rest of the body via the venous system. It added that epilepsy mainly affects phlegmatic people. It also described a pre-ictal

aura, noting that sufferers who know beforehand when they are about to be seized, and flee from men (Adam's translation, 1999).

Finally, severe anxiety was also recognised in the Greco-Roman classical period by the Stoics, who followed the Roman philosophy which advocated self-control to overcome negative emotions. Methods of managing acute anxiety resemble in many ways modern cognitive behavioral therapy. Stoics would practice a technique known as negative visualization, which involved considering the worst possible outcome of an action or event, in order to prepare the person for the consequences of it. They could recommend mentally rehearsing how they would respond to such problems and try to find a way to change negative situations into positive ones (Robertson, 2020).

4.4 Medical Schools (Sects) of Medicine at the Time of Asclepiades

In the years and centuries after the time of Hippocrates and up to the time of Galen, several competing schools (sects) of medical theory and practice emerged within the Greco-Roman world. These classical schools of medical thought and teaching were grappling with problems that have a perennial relevance to the theory and practice of medicine in any age (Johnston and Horsley, 2011). These ancient medical sets were composed of an acknowledged founder (Heresiarchs) as well as publicly identifiable leaders who often articulated their rejection of rival theories through theoretically founded polemics, as well as promoting their own systematic alternatives (von Staden, 1982; Leith, 2016).

Leith has said that “by the Roman period, it had become conventional in writing about the history of medicine to arrange the sects into three main groups: the Rationalists or Dogmatists, the Empiricists, and the Methodists. He goes on to say that the Rationalist sect was in fact a category invented by the Empiricists, comprising a variety of competing sects, united only by their general commitment to the need to discover the hidden causes of disease. The most successful of the Rationalist sects were the Herophileans, the Erasistrateans, and the Pneumatists, who were influenced by the

Stoics. However, there were many other less well-known groupings of doctors who had formed their own sects (Leith, 2016).

Many scholars of this period give the impression that these sectarian physicians (*iatroi* or *medici*) confined their medical practices to the elite of society, however Leith argues that in terms of the social status of their patients, sectarian doctors may have treated a less restricted range of the population than is often supposed (Leith, 2022).

4.4.1 *The Rational or Dogmatic School*

The Rational or Dogmatic Sect is also referred to as the Logical Sect. It had a teaching philosophy that emphasized theoretical principles. It is one of the oldest of the medical sects of antiquity. They linked reason with observation and inferred to the existence of unseen entities within the human body. They did not devote much attention to the causes of diseases but believed that a detailed knowledge of anatomy and physiology were both necessary for the physician. While there were many varieties of Dogmatism, the common characteristic was a belief in the science and the art of medicine.

Dogmatists were those who adhered to the memory of the classical medical theory as laid out by Hippocrates. As a devout follower of Hippocrates and as a Neoplatonist, Galen considered himself to be a Dogmatist. He lamented how far physicians had wandered from what he had considered the sound demonstrable system of Hippocrates in the five centuries that had passed from his day until his own.

4.4.2 *The Empiric School*

The Empirical Sect was founded in Alexandria by Serapion of Alexandria and Philinus of Cos in the middle or towards the end of the third century BC (von Staden, 2008). They rejected unobservable entities such as atoms and pores, as causes of diseases and minimized the value of anatomy and physiology as aids to the physician in treating diseases. They particularly opposed the views of the Dogmatist Sect whose emphasis was on the theoretical causation of disease (Hankinson, 2001).

They professed to derive their medical knowledge from observation and experience alone. This sect persisted up to about the fourth century AD. The doctrines of this sect are described by Celsus in his introduction to his *De Medicina* (Mudry, 1993).

4.4.3 The Methodic or Methodist School

There is no clear consensus as to who founded this medical sect. While some writers were of the opinion that Asclepiades himself may have founded this sect in c50 BC (Garratt, 1884; Yapijakis, 2009), it is now generally accepted by most modern scholars, that while Asclepiades laid the foundations of the Methodic Sect, it was Asclepiades' most distinguished student, Themison (123 BC-40 BC) born in Laodicea (in modern day Syria), who adopted and modified the teachings of his great mentor in developing what became known as the Methodist Sect (Greenhill, 1870; Boylan, 1984; Leith, 2020).

Asclepiades had taught Themison and his fellow students that the human body was composed of onkoi which were constantly moving through pores (Drabkin, 1950). There is a clear link between Asclepiades' concept of engorgement due to the blockage of the onkoi and the Methodic subsequent notion of a "state of tension in the body" (Grmek and Fantini, 2002). None of Themison's writings in relation to the Methodic School have survived except for some fragments which were preserved by the later Methodist physician and author Caelius Aurelianus (Drabkin, 1950; Moog, 1994; Tecusan, 2004).

The Methodic School classified physical diseases based on the original theory espoused by Asclepiades and divided diseases into three general types, which they called "general states" or "commonalities". Firstly, restriction of the movement of atoms (*strictura*) caused "tension in the body". Secondly, there could be laxity (looseness) of the body (what Caelius called *solutio*) and thirdly, there could be a combination of both states, which they called *complexio* (Drabkin, 1950; Dysert, 2007).

Asclepiades had previously described these three separate categories as: *status strictus*, *status laxus*, and *status mixtus* (Vallance, 1990; Nutton, 2004; Yapijakis,

2009). These three “general states” were essentially three different basic types of disease: the first, an excessively dry, tense or stringent state; the second, an excessively fluid and relaxed state; and the third, a condition involving a combination of both types of abnormality.

The Methodist physician’s treatment of disease was essentially the use of relaxing measures to counteract excessive tension and the use of astringent measures to counteract excessive laxity. When they felt that the disease was likely to be a combination case, they would combine the relaxing measures with astringents. Asclepiades had avoided the use of multiple drugs when treating a patient, in clear opposition to a trend that was particularly prominent among Empiric physicians. In this, he had some influence on the Methodists’ manner of treatments (Drabkin, 1950).

However, as he got older it appears that Themison abandoned many of the views on theoretical medicine that he had learned from Asclepiades, especially in relation to the treatment of mental illnesses. He died in 43 BC (Greenhill, 1870).

Themison was followed by Thessalus of Tralles (c70 AD-95 AD). This renowned Roman physician adopted the principles of the Methodic School and went on to modify and develop them. He was born in Tralles, which is situated in Lydia in the modern Turkish province of Uşak (Tecusan, 2004). He appeared to have a great sense of self-importance and exalted himself at the expense of his predecessors. He boasted that he could teach the art of healing in six months (Bartlett and Stempsey, 2005). Later Galen frequently mentioned him, usually with contempt. Thessalus is credited with developing a three-day medical program of therapy which he named “metasyncrisis.” His treatment was based on taking strong vegetables and emetics, accompanied by regular fasting periods (Drabkin, 1950; Bartlett and Stempsey, 2005). He wrote several medical works, of which only a few titles and a few sentences remain (Smith, 1870).

Thessalus was followed by another physician, Soranus of Ephesus who was one of the most famous physicians of the Methodic School (Hanson and Green, 1994). His systems and therapies were less radical than those of his predecessor. Soranus was a Greek physician born in 98 AD in the ancient famous city of Ephesus, situated close to Selcuk in modern day Turkey. Little is known of his life, but he practiced as a physician with a special interest in gynecology, obstetrics, and paediatrics.

Soranus is probably best known in modern times as the author of *Gynaecaea* (“On Gynaecology”), and his treatises on obstetrics and paediatrics. His work comprised four books, which also contained sections on fractures and bandages, as well as on many other aspects of surgery. In addition, he included a brief section on the life of Hippocrates. Arguably, Soranus’s greatest works were his two treatises on various diseases and their treatment, *De Morbis Acutis et Chronicis* (“On Acute and Chronic Diseases”), which included “On Acute Diseases” (three books) and “On Chronic Diseases” (five books). All were written in Greek.

Soranus severely criticized his predecessor Themison for his cruel handling of patients with mental difficulties which had included placing patients in chains, often in dark confinement, deprived of food and water. Soranus also took a critical review of the harsh methods forwarded by Roman physicians of the time in treating mental illnesses. Like Asclepiades before him he advocated techniques that utilized kindness and generosity (Nutton, 2004).

Tradition holds that Soranus was educated in Alexandria and Nutton says this would have accounted for his anatomical knowledge (Nutton, 2005). Soranus’ writings defined medical opinion concerning women’s diseases, pregnancy and infant care for nearly 1,500 years. He was a prolific writer who published widely on a variety of medical topics as well as on philosophy. Several of his writings still survive, most notably his four-volume and his *magnum opus*, *De Morbis Acutis et Chronicis*. Dysert has said that Soranus’ writings indicated that he had broad historical, philosophical, and medical interests as well as having great familiarity with other schools of medical thought. In his “On Acute Diseases” Soranus he was emphasizing aspects of the practice and theory that are specifically Methodistic. He drew a sharp distinction between acute and chronic diseases as well as the relative importance of anatomy. He also took a holistic view of human disease but was not averse to entertaining other theories and explaining them (Dysert, 2007).

It is widely accepted that Methodism arose in reaction to both the Dogmatic (Rationalist or Logical) and Empiric Schools. Methodism does bear certain similarities to both schools, and Sextus Empiricus pointed out some common ground between Methodism and the much earlier School of Pyrrhonism (Skepticism), although

Methodism was also different in significant ways (Hankinson, 1987; Dysert, 2007). In any case, the Methodic School, which was primarily a Roman phenomenon, soon became a new method of medical treatment. It was opposed by traditional Dogmatists and Empiricists who pilloried the Methodists for what they considered to be the loose logic of their so-called methodological revolution, especially their socially disruptive claims to be able to teach medicine in six months.

However, the popularity of the Methodists was due in large part to them being able to provide a ready supply of medical practitioners, as well as their focus on providing rapid therapeutic outcomes. As the Methodic school developed, its main priority was to observe some general symptoms of a patient in order to decide on the proper and appropriate therapy for the patient. The Methodists denied that medicine should be based on “hidden cases” such as humors, atoms, or elements. They argued that the inner workings of the human body were ultimately unknowable, and as such lay beyond the limits of human knowledge and inference. Consistent with this, they placed very little emphasis on human anatomy (Webster, 2015). The Methodic school emphasized that it was the treatment of the disease that was the most important aspect of patient management, rather than its causes or the medical history of the patient. They argued that knowledge of the cause of any disease bears no relationship to the method of the cure. They postulated that all the Methodic physician needed to know was how to make a diagnosis of the patient’s disease, and the subsequent treatment of the disease would be based on observation and recourse to lists of previous clinical case histories, and from this knowledge alone, the correct treatments would follow.

In summary, Methodic medical practice was known for its deprecation of the theory of causation of disease in favor of therapeutics.

4.4.4 *The Asclepiadean School*

We must rely on the writings of others as to whether in fact Asclepiades formed a medical school (or sect). Pliny refers to him as having formed a distinct entity which he called a *Nova Secta*. However, there is no evidence of, or reference to, this by Crassus or other contemporary writers (Flemming, 2012). Pliny also refers to four

physicians who were Asclepiades' pupils namely, Themison of Laodicea, Tilus Aufiduis of Sicily, Philonides of Dyrrachium, and Nico of Agrigentum (Pliny, HN 29.6 and Caelius Aurelianus SP284). All of Asclepiades' followers, with the noticeable exception of Themison, remained loyal committed to the pathophysiology therapeutics of their teacher and mentor, which was based on the onkoi and poroi theory of the body's particulate situation, process, and interactions (Flemming, 2012).

In a recent article, David Leith refers to Asclepiades' complex relationship with his pupil, the founder of the Methodist Sect Themison of Laodicea, and noted that at times that this led to the mistaken impression that his medical views were somewhat swallowed up by Methodism and thus were superseded (Leith, 2020). In the same article Leith also refers to John Vallance's studies of Asclepiades medical theory, where Vallance seems to be almost unaware of an Asclepiades's sect.

Leith argues that in fact Asclepiadean medicine continued to be practiced in its original form for at least 150 years after his death (Leith, 2020). Leith goes on to quote Seneca (c4 BC- 65 AD), the Roman Stoic philosopher, historian and statesman, when writing in the mid-first century AD said "now add to this the fact that many arts, indeed the most liberal of all-also have their own doctrines, and not just precepts, such as medicine: thus the sect of Hippocrates is different from that of Asclepiades, which is different from that of Themison (Leith, 2020).

Leith refers to several notable physicians who were loyal followers of Asclepiades. Philonides of Dyrrachium was a significant follower and pupil of Asclepiades of Bithynia. He most likely travelled to Rome to train under Asclepiades and had a distinguished medical practice in his ancient homeland city of Dyrrachium on the Adriatic coast near the modern-day city of Durres in Albania. He remained loyal to his master and was a prolific writer on medical topics, having written forty-five books. Another important pupil of Asclepiades was Nikon of Acragas, an ancient Greek city on the current site Agrigento Sicily. Other notable Asclepiadean physicians included Marcos Artorius of Smyrna in modern-day Izmir Turkey and the physician Lusius (Leith, 2020).

Leith has pointed out that these Asclepiadean students, especially Philonides, were important indicators of the early spread of Asclepiadean medicine outside of the

city of Rome (Leith, 2020). Leith further adds that these members of the Asclepiadean School (sect) continued to be associated with the highest levels of Roman power, with two notable physician followers, Marcus Artorius and Antonius Musa, both being personal doctors of the Emperor Augustus, and both are believed to have saved his life on separate occasions (Leith, 2023).

Leith summarizes by saying that the Asclepiadean sect, notwithstanding Galen's selective silence, was eventually a significant force on the medical scene of the first century BC and AD, spreading beyond Rome to cities such as Dyrrachium. Such connections with the Roman elite suggest that Asclepiades's followers continued to act as important vehicles for the secure installation of Greek medicine in Rome during the first century BC (Leith, 2020).

4.5 Asclepiades' Supporters and Detractors

Asclepiades had both supporters and detractors. His supporters included Antiochus of Ascalon, Cicero, Lucius Crassus, Philodemus of Gadara, Strabo, Pedanius Dioscorides, Aulus Cornelius Celsus, Scribonius Largus, and Apuleius. His detractors included most notably Pliny the Elder and Aelius Galenus. All merit attention.

4.5.1 Supporters of Asclepiades

Antiochus of Ascalon (c.120 BC- c68 BC) was a Greek Platonist-Skeptic philosopher. Sextus Empiricus, who lived in the second or third century AD, mentions in *Adversus Mathematicus* that Antiochus may have been acquainted with Asclepiades when they were both living in Athens (Floridi, 2002). Antiochus was a philosopher in Plato's fifth Academy and had a considerable reputation in ethics and epistemology. He was also the teacher of Cicero. Antiochus was born in c120 BC in the city of Ascalon in ancient Palestine. He studied in Athens and Alexandria, as well as in Syria. In his *Canonica*, Antiochus refers to "a certain other man, second to none in the medical art, and also a student of philosophy who believed that all sensations are really perceptions, and that we apprehend nothing at all only by reason" (Floridi, 2002). Sextus Empiricus

suggested that Antiochus referred here to Asclepiades of Bithynia. Flemming argues that both Antiochus and Asclepiades were important participants in the changing intellectual and political world of the late Hellenistic Mediterranean, a world that was being reshaped by the increasing power of Rome. Both spent time in Rome, Asclepiades settling there, and both were drawn into the wider network of Roman elite patronage and influence. Moreover, Asclepiades' choice of the emerging metropolis as his base at the expense of Alexandria, the established base of the Mediterranean, finds a parallel of a kind in Antiochus' displacement from Athens, the historic home of the philosophical schools, to the less philosophically developed Egyptian capital as well as other cities of the East (Flemming, 2012).

Whether Cicero (106 BC- 43 BC) met and knew Asclepiades is open to question. Cocchi and Rawson have argued that this is somewhat unlikely given their age differences (Cocchi, 1758; Rawson, 1982). In his famous *De Oratore*, Cicero states that Lucius Crassus (140 BC- 91 BC), the noted orator and Roman general of consular rank "enjoyed his (Asclepiades) services as a friend and doctor in the past" (Tempest, 2013).

Philodemus of Gadara (c110 BC - c35 BC) was an Epicurean philosopher and poet who was born in the ancient Greek city of Gadara, which is situated in present day Jordan. In Athens, Philodemus studied philosophy under Zeno of Sidon before moving to Rome to teach (Clay, 1998; Tosun, 2007). He was not a physician. He subsequently lived in the mediterranean port city of Herculaneum, residing in the wealthy Epicurean senator Calpurnius Piso's villa that housed the great Papyri Library of Philodemus, that was somewhat conserved by incomplete burning during the volcanic eruption of Vesuvius in 79 AD (Yapijakis, 2022). Percy has suggested that Philodemus most likely met and knew Asclepiades while they were both in Rome, as they were both near contemporaries. Both were Epicureans and Greek intellectuals with patrons in the Roman governing class of that period and would have had many common interests (Percy, 2012).

Strabo was a Greek Stoic philosopher and historian who was born in 64 or 63 BC in the city of Amasia on the Pontus situated in present day Turkey. He lived during the transitional period of the Roman Republic into the Roman Empire (Purcell, 2017). He

travelled widely around Greece before moving in 44 BC to Rome where and he stayed for the rest of his life, studying and writing. Strabo referred to Asclepiades as “the worthiest of Bithynian men in respect to education” (Gumpert, 1794; Clarke, 2012). Similarly, Pedanius Dioscorides (c40 AD- c90 AD), a Greek Methodic physician, botanist, and pharmacologist, recorded in his *De Materia Medica* that many of his major drug sources were Asclepiadean.

Aulus Cornelius Celsus (25 BC- AD 50), was a distinguished Roman encyclopedist who held Asclepiades in high esteem. He composed his famous eight-book treatise *De Medicina* in the early first century AD. This monumental work was written in Latin and is considered by many to be the first and probably the best book on medicine of that time. *De Medicina* is a primary source on diet, pharmacy, surgery, and related fields. This magnum opus has made a significant contribution to ancient medicine, especially on the on treatments of skin diseases. Lost portions of this encyclopedia likely included volumes on agriculture, law, rhetoric, and the military arts (Green, 1955). Celsus was an intellectual polymath. It is unclear if he was a physician. Celsus had a qualified positive attitude towards Asclepiades. He said that Asclepiades “by his concentration on ‘dietetics’, the healthy regime as opposed to pharmacology or surgery, [had] introduced an entirely new epoch” (Celsus proem. I; Mudry, 1993). In his *De Medicina* Celsus mentioned that he held Asclepiades “in high esteem” and referred to him as “a good author of many things which he himself had achieved”. Celsus added that “he valued himself as being a follower of Asclepiades”. Why Pliny does not mention Celsus or take any account of his medical encyclopedia, is difficult to understand. Could this have been due to the fact that Celsus was a Roman? It should be noted that Pliny is quoted as saying that “very few Romans had touched such a subject” (i.e., medicine) (Pliny, H.N. XXIX, capI.). Not only is this surprising, but it is simply untrue.

Scribonius Largus was a Roman pharmacologist and court physician to the emperor Claudius. He was born in 1 AD and died around 50 AD. In 47 AD, at the request of Caius Julius Callistus, who was an Imperial Official and the Emperor’s freedman, Scribonius drew up a list of 271 medical prescriptions which he produced in his major work: *Compositiones Medicamentorum*. In one passage of his book, he

described “Asclepiades’ pills [as] the best preparation for artery trouble”. He goes on to refer to Asclepiades as “one of his own and the great author of medicine” (Cocchi, 1758; Sconocchia, 1983; Hamilton, 1986; Bernhold, 2011; Cambiaghi and Sconocchi, 2018). Sadly, later in the fifth century AD much of Scribonius’ great work was appropriated by Marcellus Empiricus without any acknowledgement to the original work of Scribonius.

Apuleius was a Numidian, Latin-language prose writer, Platonist philosopher, and rhetorician (Harrison, 2004). He was born in 124 AD in the Berber city of Madauros in modern day Algeria. He died around 171 AD. In his book “Florida”, he wrote that Asclepiades “was chief among the most famous of physicians” (Apuleius, Florida, 19.B.IV.; Lee, 2005).

Pliny mentioned that Asclepiades rescued a live man who was thought to be dead from his own funeral bier (Pliny NH 7.124; Rawson, 1985). Yapijakis has postulated that Asclepiades most likely had noticed that the presumed dead person was not really deceased and he ‘revived’ him to the amazement of everybody around (Yapijakis, 2009). This is unverifiable, but even if apocryphal, it indicates the esteem in which Asclepiades was held by his many supporters

4.5.2 *Detractors of Asclepiades*

Asclepiades had a number of detractors including, most notably, Pliny the Elder and Aelius Galenus (Galen).

Pliny the Elder (23 AD -79 AD)

Gaius Plinius Secundus (Pliny the Elder) was born in either 23 AD or 24 AD, into a wealthy aristocratic equestrian family in Cisalpine Gaul (Northern Italy) during the reign of the emperor Tiberius. The family had strong political connections in Rome. Pliny was considered to have been an eccentric workaholic who never married or had any children. At the age of 23 years, Pliny began a military career, while at the same time as studying law. In 47 AD he went with the Roman army as a cadet to fight in Germany.

He rose rapidly through the army ranks to obtain the post of commander of a cavalry wing. He was already writing extensively during this period. On his return from Germany, he took up residence on the Equiline Hill in Rome, where he tired of practicing law, he devoted most of his time to writing. He was a prodigious author and combined his scholarly activities with a busy career as an imperial administrator (procurator) for Emperor Vespasian, who became a great friend (Wasson, 2014).

Pliny's most famous production was his "Natural History". This magnum opus was published in 77 AD. This monumental work is divided into 37 books organized into 10 volumes. This immense undertaking, which Pliny began in c77 AD still survives, encompassed a wide variety of topics. Some historians view Pliny's "Natural History" as the first ever encyclopedia (Rackham et al, 1938; Doody, 2009). Pliny's sources were his own personal experiences as well as extracts from the works of others, which he collected in the following manner: one of his servants would read to him aloud and another one would then write down the extract as dictated by Pliny (Beagan, 1992; Dennis, 1995; Doody, 2010).

In his "Natural History", Pliny has provided us with most of our knowledge on Asclepiades, albeit much of it written in a biased and frequently sarcastic manner. While Pliny was not a physician, his Books 20 to 32 deal exclusively with medicine and medical topics (Bostok and Reilly 1857; Reynolds, 1986).

Like Cato before him, Pliny had a personal bitterness and irreconcilable hostility towards all Greek physicians, which undoubtedly explains his deliberately vindictive, and often distorted image of Asclepiades of Bithynia (Benedum, 1967; Nutton, 2005; Yapijakis, 2009; Leith, 2019). For example, Pliny claimed that when Asclepiades first came to Rome, he was an impoverished teacher of rhetoric and only turned his hand to

medicine, with no knowledge of drugs, to make money. He also said that while in Rome, Asclepiades was chiefly known for his learning and eloquence rather than for his medical knowledge. He said that Asclepiades was a single man who came from a most trivial nation and was setting himself to the undertaking, without knowledge, to be able to give the laws of health to the human race (Pliny, NH. book 26). He frequently pilloried Asclepiades' agreeable treatment methods which he said amounted only to the pampering of his wealthy patients (Natural History book 26. chapters 12-15).

Flemming notes that paradoxically when Pliny was describing Asclepiades for the first time in his "Natural History", he said that Asclepiades is hailed as the most outstanding figure ever in the art of medicine, outstripping even Hippocrates himself (NH book 7, 123-4). However, Flemming adds that the large-scale changes that Asclepiades wrought will be later lambasted by Galen in the rest of the work that Pliny wrote in "Natural History". Flemming goes on to say that Asclepiades is the chief villain in the Pliny's Roman medical history, a fact that emphasizes, rather than diminishes his impact" (Flemming, 2012).

In an important recent publication, Leith convincingly refutes the basis of Pliny's hostility towards Asclepiades. Leith provides a detailed comparison between what Celsus reported about Asclepiades' therapeutics in his *De Medicina* and what Pliny said about Asclepiades' treatments in his "Natural History" and concludes that Pliny was clearly manipulating the information he obtained from Celsus's work in highly misleading and selective ways. Accordingly, Leith suggests that contradictory and competing accounts should be given greater emphasis. Leith goes on to say that what Pliny has said about Asclepiades' approach to therapy has had a highly adverse impact on modern assessment of Asclepiades and that his use of Celsus demonstrates that he had little interest in trying to understand Asclepiades' therapeutics in general, or indeed in representing it accurately as a whole. Leith notes that many of the details recorded by Pliny about Asclepiades' therapy are in direct conflict with our more detailed sources. Leith goes on to say that comparison with his Celsus source often enables us to understand how Pliny has distorted his data. Leith Concludes by saying, "for reliable material on Asclepiades' approach to therapy, we should

as a rule, look elsewhere than book 26 of Pliny's "Natural History" (Leith, 2019).

Pliny's overarching campaign against Greek medicine was paramount for him, casting critical doubt on his portrait of Asclepiades as greedy, inexperienced, and pandering. For reliable material on Asclepiades' approach, Griffen has also pointed out that Pliny's overall assessment of Asclepiades is in stark contrast to his relatively tolerant treatment of other Greek philosophers (Griffen, 2007). Many scholars have queried why Pliny should have been so spiteful towards Asclepiades. It was Cocchi's view that Pliny's anger towards Asclepiades might have been due in part to jealousy and envy (Cocchi, 1758). Interestingly, Rawson has raised the possibility that some of Pliny's attacks on Asclepiades may have been due to Pliny confusing him with Asclepiades of Myrlea, a noted grammarian and rhetorician who came to Rome in the time of Pompey (106 BC-48 BC) to teach the art of grammar and oratory, before subsequently relocating to Alexandria and finally settling in Spain. Like Pliny, Asclepiades of Myrlea was not a physician (Pliny, NH, 2.20; Susemihl, 1892; Rawson, 1982; Bowie, 2014). It needs to be noted that Pliny was not always so consistently negative about Asclepiades. He did praise him on occasion writing that "the greatest renown belongs to Asclepiades of Prousius for founding a new sect, for spurning the envoys and promises of extreme riches of King Mithridates to be the king's physician adding, that Asclepiades' decision to stay in Rome was very well received by the Romans" (Pliny, HN.7.3). Pliny also wrote, possibly sarcastically, that Asclepiades had developed a method for curing the sick with wine, for dragging down a man from his own funeral procession and saving his life, but most of all for having made a wager with fortune, that he would not be a doctor if he ever fell ill in any way. And he won, having died in extreme old age by falling down some stairs. Leith concludes that Pliny had little interest in trying to understand Asclepiades' therapeutics in general, or in representing it accurately as a whole (Leith, 2019).

In August of 79 AD, all of Italy was shocked when Mount Vesuvius erupted, destroying the cities of Pompei, Herculaneum and Stabiae in a volcanic inferno. At the time of the eruption, Pliny was serving as an Admiral of the Roman naval fleet based off nearby Campania. His intense scientific curiosity and perhaps his natural compassion led Pliny to conduct rescue efforts for the evacuation of the citizens of

Pompeii. Unfortunately, his valiant efforts led to his death a day after the cities of Pompeii and Herculaneum were destroyed by the volcano. There is some debate as to whether he was on a Stabiae beach or possibly on his boat. It is a matter of dispute as to precisely how Pliny died. Most scholars are of the view that he most likely died on the beach of Stabiae by the inhalation of the volcanic toxic fumes. Zirkle however, has said the Pliny most likely died of a heart attack, as the sailors around him were not killed (Bigelow, 1859; Zirkle, 1967; Doody, 2010; Wasson, 2014).

Galen (129 AD-216 AD)

Asclepiades' other chief detractor was Aelius Galenus or Claudius Galenus (often anglicized to Galen or Galen of Pergamon), who was an illustrious Greek physician, surgeon, and Neoplatonic philosopher. Galen was also a prodigious writer, who was perpetually inquisitive, even in areas remote from medicine such as logistics (Daremborg, 1853). Pergamon was renowned for its Temple to Asclepius. Galen is generally considered to be one of the most accomplished and influential medical researchers of antiquity. His views on medicine dominated and influenced Western medical science for more than 1,300 years up to the mid-seventeenth century in Europe, as well as having a major influence in the Byzantine and middle eastern medical worlds. Galen was born in Pergamon in modern day Turkey in 129 AD. He was the son of Aelius Nicon, a wealthy architect and builder, who, around 145 AD, supposedly had a dream in which Asclepius appeared to him and commanded him to send his son to study medicine (Nutton, 2005). When he was 16 years of age, Galen began his medical studies at the Asclepium in Pergamon under the tutelage of the Greek physicians Aeschnion, Stratonicus, and Satyrus. Galen subsequently travelled widely. In 162 AD he moved to Rome, where he established a considerable reputation before returning to Pergamon in 166 AD. In 168 AD he was called back to Rome by the joint emperors Lucius Verus and Marcus Aurelius in order to accompany them as their chief physician to the Roman army which was embarking on a military campaign to Northern Italy and Germany.

Galen was a prodigious writer. His extant works are to be found in his *De Naturalibus Facultatibus* (“On the Natural Faculties”), a monumental undertaking comprising three books (Brock, 1916; Singer, 2008; Johnston, 2009). Galen’s medical writing encompasses almost every aspect of medical theory and practice of his era. In addition to summarizing the state of medicine at the height of the Roman empire, he reports on his own advances in anatomy, physiology, and therapeutics. As Galen’s teachings were compatible with developing Christianity, his medical scholasticism managed to survive, despite the discoveries of the Renaissance, right up to the seventeenth century.

Galen regarded anatomy as the foundation of all medical knowledge. Many scholars have taken the view that his advocacy of animal dissection for teaching surgical skills and for research purposes formed part of his self-promotion. He was an astute clinical observer, who accurately distinguished the differences between sensory, motor, and mixed nerves. He also distinguished and identified seven pairs of cranial nerves. While publicly dissecting a live pig in front of a public audience, he produced a hemiplegia by sectioning the pig’s spinal cord and caused aphonia by cutting the recurrent laryngeal nerve of the squealing pig. He also described the valves of the heart and the difference between arteries and veins. One of the most important outcomes of his demonstrations was that he described that arteries were the carriers of blood, and not air (pneuma), as had been taught for the previous 400 years.

Galen’s physiology was a mixture of ideas taken from the teaching of the philosophers Plato and Aristotle. He revered the work of Hippocrates. Galen viewed the human body as comprising three interconnected systems: first, the brain and nerves, which were responsible for sensation and thought, second, the heart and arteries, which he felt were responsible for life-giving energy; and third, the liver and veins, which he said were responsible for nutrition and growth. According to Galen, blood was formed in the liver and then carried by the veins to all parts of the body where it was used as nutriment or transformed into flesh and other substances. Galen suggested that a small amount of blood would seep through the lungs, between the pulmonary arteries and the pulmonary veins, and this seeping blood would become mixed with air, before passing from the right ventricle on to left ventricle of the heart through minute pores in the

septal wall separating the two cardiac chambers. He also suggested that a small portion of this blood would be further refined in a network of nerves at the base of the skull, allowing the brain to make what he called the “psychic pneuma”, which he described as a subtle material that he claimed was the vehicle for all human sensations.

Galen’s physiological theory proved extremely seductive to those studying medicine at the time, and few possessed the skills needed to challenge his theories in the succeeding centuries. As Galen’s medical theories were mainly based upon the philosophy of Aristotle, they were generally accepted by developing Christianity, and so his teachings remained essentially unassailable for centuries. While Galen was a strong supporter of the Hippocratic four humoral approach to medicine, he modified the classic Hippocratic theory by arguing that the humoral imbalances responsible for disease could also be located in specific organs in the human body, as well as the body as a whole. This modification of the traditional Hippocratic method allowed Galenic physicians to make more precise diagnoses and prescribe specific remedies to restore the body’s balance of the humors.

In his *Naturalibus Facultatibus*, Galen vigorously attacked all of those who had previously supported the physiological atomic theories of medicine. In particular, he rejected what he called “the absurd molecules of Asclepiades” (Vallance, 1993). As a staunch supporter of the Hippocratic humoral theory of medicine, he treated with contempt and ridicule the mechanistic theories of Asclepiades and those of the subsequent Methodic school (Horne, 1963). However, while he was contemptuous of the methodist Thessalus, he did hold the methodist Soranus of Ephesus in high regard (Drabkin, 1950).

Galen was particularly vitriolic towards Asclepiades. In his chapter in the *De Theriaca ad Pisonem* he intentionally connected Asclepiades to a traditional form of Abderite atomism. He did this to sarcastically show that Asclepiades’ theories should then be viewed as ridiculous. One of Galen’s most favored arguments against the onkoi of Asclepiades (see later in this thesis) was that they were unable to account for the phenomena of pain, as onkoi themselves are without sensation (Leith, 2009). Galen also attacked Asclepiades on a personal level, accusing him of being boastful, arrogant and frequently self-contradictory (Rawson, 1982).

Galen, as a human anatomist, was outraged by Asclepiades' anatomical ignorance in believing that the human bladder acted like a sponge. According to Asclepiades' particle physics theory, there are no impermeable structures within the human body. He was saying that when urine is produced in the kidney it makes its way to the bladder and then passes through micro-porous channels into the bladder. Galen, as a human anatomist, was outraged by Asclepiades' anatomical ignorance in believing that the bladder acted like a human sponge (Gal. *De Naturalibus Facultatibus* 1.13 {11.30-35k.}).

Vallance contextualizes these attacks by Galen on Asclepiades, stating that while much of Galen's writing was directed against Asclepiades, it was also a fact that Galen aimed his ire against most of his contemporary medical rivals at the time (Vallance, 1990). Grmek has pointed out that if Galen idealized the figure of Hippocrates and extolled the worth of his medical treatises of the classical age, he did so to combat more effectively all doctrines that were opposed to his own (Grmek, 1988). Leith adds that Galen's tendentiousness in reporting or interrupting the views of his predecessors, doctrinal friends and enemies alike, must generally be treated with caution (Leith, 2012). Leith's views on Galen are shared by many others (van Staden, 1997; Allen, 2001; Tecusan, 2004; Yapijakis, 2009).

However, Galen's writings achieved wide circulation during his lifetime and copies of some of his works that were written within a generation of his death have survived to this day. By 500 AD, Galen's works were being taught and summarized at Alexandria and his theories were already crowding out those of others in the medical handbook of the Byzantine world. Greek manuscripts began to be collected and translated by enlightened Arabic scholars in the ninth century. Around 850 AD, Hunayn ibn Ishaq, an Arab physician at the court of Baghdad, prepared an annotated list of 129 works of Galen that he and his followers had translated from Greek into Arabic. Learned medicine in the Arabic world thus became heavily based upon the commentary, exposition, and understanding of Galen's teaching. Galen's influence was initially negligible in western Europe, except for his drug recipes. However, from the late eleventh century onwards, Hunayn's translations and commentaries by Arab physicians, and sometimes the original Greek writings, started to be translated into

Latin. These Latin versions came to form the basis of medical education in the evolving European medieval universities. A copy of *De Naturalibus Facultatibus* appeared in London in 1523. Galen's "new followers" stressed his methodical techniques of identifying an illness, his independent judgement, as well as his cautious Empiricism. Galen's instructions to investigate the body were eagerly followed.

Physicians were now being encouraged to repeat his experiments and observations that he had recorded. Paradoxically for many of his followers, this ultimately led to the overthrowing of Galen's authority as an anatomist. In 1543, the Flemish physician and anatomist Andreas Vesalius showed that Galen's anatomy of the body was more animal than human in some of its aspects. It became clear to his medieval followers that Galen had made many human anatomical errors. By contrast, Galen's notions of human physiology lasted for a further century, until the English physician William Harvey correctly explained the circulation of blood. Arthur John Brock translated Galen's three books from the original Latin into English. The English version of "On the Natural Faculties" was subsequently deposited in the Loeb Classical Library (Brock, 1916).

Most of Galen's polemic views on Asclepiades are contained in Book 1, but Asclepiades is also mentioned in Books 2 and 3. Galen is generally scathing, sarcastic and generally dismissive of the theories and practices that Asclepiades had been promulgating were now appearing in the English language.

Galen consistently and vigorously attacked all the ancient physiological atomic theories but especially those that had been posited by Erasistratus and Asclepiades.

4.6 Atomism in the Middle Ages

According to Gregory, Asclepiades' theories and atomism in general were not the dominant medical theories accepted in the European Middle Ages (Gregory, 1931). While this is generally true, there were some rare expressions of interest in atomic philosophy during this period. For example, Nicholas of Autrecourt, a French philosopher and theologian (1299- 1369), considered that all matter, space, and time were all made of indivisible "atoms", which he referred to as "points and instants".

According to Dutton, the views of Nicholas were very similar to those that had been proposed earlier by the great Muslim theologian and mystic al-Ghazali (1058- 1111) (Dutton, 1996). Aristotelian physics had broadly held sway in the universities of Europe for most of the Middle Ages, even through to the time of Newton.

The Renaissance was a period of European cultural, artistic, and economic rebirth and is generally described as covering the period of the fifteenth and sixteenth centuries. During this time, other physical theories were gradually being introduced to many university curricula (Kargon, 1966). Some of the main contributors to the rebirth of atomic theory at this time included Isaac Beckman, Francis Bacon, Giordano Bruno, and Thomas Hobbes (Clericuzio, 2000).

Galileo (1564- 1642) posited a more complete physical system which he based on a corpuscular theory of matter in which all phenomena, except for sound, were produced by “matter in motion.” When Galileo rejected Aristotelian philosophy and supported atomic theories of matter, it put him at odds with Christianity (Redondi, 1969).

The Dutch philosopher Isaac Beckmani (1588- 1637), who was also a scientist and physician, developed a theory of matter based on the concepts of ancient Greek atomism. While he did not publish any of his ideas, he kept an extensive diary which he called the “Journaal”. His brother published this posthumously in 1641. Beckmanni’s “Journaal” remained dormant until it was rediscovered in 1905. It was then noted that Beckmanni had worked on theories which were very similar to those being posited by the Greek philosophers and physicians some 2,000 years previously (Beckmanni, 1644).

Despite these often-controversial contributions in the sixteenth and seventeenth centuries, atomism was not fully revived until René Descartes (1596-1650) and Pierre Gassendi (1592-1655) published their new physic systems, based on an atomic theory. In the case of Gassendi based on an atomic system, and in the case of Descartes based on a corpuscular theory. Descartes was a noted French philosopher, mathematician, and scientist. He has been described as the father of modern philosophy (Gaukroger, 1995). Descartes was one of the key figures in the European Scientific Revolution of the seventeenth and eighteenth centuries. Amongst his enormous contributions to

philosophy and science, Descartes was positing, just as Asclepiades had suggested two Millennia earlier, that the physical universe was composed of “divisible corpuscles” of matter. Interestingly, Descartes did not believe in a void space (Gaukroger, 1995; Clarke, 2006). Grundy had earlier argued that Descartes was not atomist, in the true sense of the word and classed his theory as one of mechanical cosmology, because the main difference between atomism and corpuscularism was the existence of the void (Grundy, 1954).

At around the same time, Pierre Gassendi, a French Catholic priest, theologian, mathematician, and astronomer, endeavored to reconcile Epicurean philosophy (atomism) with Christianity. He sought to “purify” atomism from its heretical and atheistic philosophical conclusions, but his studies on atomism contained many contradictions and did not have any enduring influence (Fisher, 2005, Yapijakis, 2022).

Towards the end of the eighteenth century, developments in the sciences of engineering and technology started to influence philosophical explanations of the composition of matter. Mathematicians who speculated on the ultimate nature of matter were now also seeking to verify their ideas through objective experiments.

Roger Joseph Boscovich (1711-1787) was a Jesuit mathematician, astronomer, and physicist was born in Dubrovnik in the then Republic of Ragusa (in modern-day Croatia). In 1758 he published his most famous work, *Philosophiae Naturalis Theoria*, which presented the first general mathematical theory of atomism. Boscovich’s work was based on the ideas of Isaac Newton (1643- 1727) and Gottfried Leibniz (1646-1716). Boscovich’s atomic theory had great influence on the nineteenth and twentieth century theoretical physics thinking (Fitzpatrick and Fitzpatrick, 1968).

Boscovich’s theory eliminated the Democritian-Newtonian dualism of particle and void space, substituting a monism of spatial relations. He was positing that physical structure was a three-dimensional pattern of what he called “point atoms.” These were subsequently described by Faraday (1791- 1867) as mere “centers of force and not particles of matter” (Weinberger, 2013). Boscovich was impelled to his task by three great agencies, the tradition of atomism, the principle of quality, and the Newtonian concept of force (Whyte, 1961).

A further development in atomic thinking occurred with the arrival of John Dalton (1766-1844), an English physicist, chemist, and meteorologist. Dalton assimilated the known experimental work of many others and produced empirical evidence about the composition of matter. He formulated the principle that each chemical element was composed of identical atoms. For example, he noticed that distilled water everywhere, when analyzed, was composed of the same elements: hydrogen and oxygen. Similarly other purified substances decomposed to their same basic elements and in the same proportions and weight. Dalton proposed several laws, which became collectively known as Dalton's Atomic Theory or Daltons Laws (Rocke, 2005).

In this way, these developments came to underpin current understandings of basic elements and, thus, much of modern science. This intellectual history accords a prominent position to the contributions of Asclepiades of Bithynia as an element in the evolution of these ideas which remain foundational to modern scientific thought.

Chapter 5: Conclusions

This chapter in the thesis presents overall conclusions from previous chapters (Section 5.1) and outlines useful directions for future research into Asclepiades of Bithynia and his work, especially in the context of modern medicine (Section 5.2).

5.1 Overall Conclusions

5.1.1 Asclepiades' Contribution to Modern Medicine and Surgery

Religious and magical beliefs had dominated the minds of humans until in the sixth century BC, when philosophy started to flourish in the Greek cities of the Aegean islands and the nearby Ionian coast of Asia Minor (Yapijakis, 2009). These Greek philosophers were attempting to explain Nature using their experience based on the senses, as well as their imagination based on empirical analogies and rational assumptions (Porter, 1996; Farrington, 2000). As Yapijakis has said, it was precisely this environment of intellectual freedom that allowed scientific medicine to be born (Yapijakis, 2009).

Hippocrates of Kos based his view on medicine on the philosophical idea that Nature was composed of four basic elements of: water, earth, wind and fire, as well as the four elemental conditions of: cold, hot, dry, and moist. Analogous to these four concepts, Hippocrates postulated that the human body consisted of four fluid humors, which he called: black bile, yellow bile, phlegm, and blood. He was saying that good health existed when these four humors were in balance, while disease on the other hand was due to an imbalance of these four humors. Hippocrates was advocating that the physician had to aim to re-balance humors, in order to facilitate the healing work of a benevolent Nature (Yapijakis, 2009). This became the standard approach to the practice of medicine of the time in the Roman world. The Hippocratic belief in the four-humor theory and its benevolent nature axiom was later reinforced by Galen of Pergamon in the second century AD and later influenced Christian and Muslim physicians up to the Middle Ages.

When Asclepiades arrived in Rome in the late second century BC, and having been greatly influenced by Epicurean philosophy, he brought with him a revolutionary physio pathological theory of human disease that boldly challenged, and rejected, the existing Hippocratic doctrine of the four humors and its benevolent nature axiom (Edelstein, 1967).

Asclepiades sought to construct a new physio-pathological theory of human disease causation which was derived in part on the philosophical atomic theories of chance and evolution which had been described earlier by Leucippus, Democritus and Epicurus. Asclepiades was not an atomist in the traditional sense of the word, as his theoretical particles of matter (*onkoi*) were not finite and indestructible but were capable of being broken into smaller particles that could assume a myriad of different shapes and sizes that would aggregate and form larger complex compounds of matter that would ultimately compose all of the varied components of the human body. He was theorizing that all this motion and aggregation was occurring within a void space with channels and pores. Leith has called this system of a void and pore complex, a void interstice (Leith, 2020).

According to his medical theory, Asclepiades was saying that health was maintained by the free, unimpeded, and balanced movement of the *onkoi* through these theoretical pores, while disease occurs as a consequence of a blockage or a constriction of the pores which would result in an interference with the smooth passage of the *envoi* through the pores at particular sites in the body resulting in different types of disease entities.

As Leith has said, it is worth noting that Asclepiades' interest in elemental theory was in itself a highly unusual topic for a doctor at this time. He is the only physician we know of in the Hellenistic period who thought that knowledge of the elements of things had any relevance to medicine at all. Most of his predecessors and successors, at least before Galen, were united in believing that a knowledge of the elements was irrelevant and belonged properly only to natural science. These physicians were not skeptical about the inquiry into the elements, they merely believed it did not properly fall within the domain of medicine as a discipline. Asclepiades'

striking deviation from his rivals in this regard is due in large part to the deep influence of Epicurean science on his thinking (Leith, 2020).

Asclepiades' contribution to modern Medicine and Surgery was significant in many ways:

Modern Molecular Medicine

Asclepiades was among the first to challenge the long-standing Hippocratic theory of the four humors. This was a bold move that set the stage for alternative theories of medicine, diverging from the dominant medical paradigms of his time. He introduced an innovative mechanistic theory of medicine based largely on Epicurean atomism. His theory proposed that the human body was composed of tiny imperceptible particles which he called onkoi which moved about constantly in a void space.

Asclepiades onkai/void/pore theory is surprisingly modern in its concept. His theoretical fragmented onkoi could be viewed as being conceptually like modern atomic particles known as quarks that exist within the neutrons and protons of the modern sub-atomic nucleus (Close, 2004). On the other hand, it appears more probable that Asclepiades' onkoi were molecules (composite bodies made of atoms) and the fragmenta were parts of broken onkoi (Yapijakis, 2009 and 2017). Health according to Asclepiadean theory was the result of the free and balanced movement of these onkoi through micro-pores and channels, while disease resulted from blockages. As Yapijakis has stated, diseases are caused by alteration of form, position or free flow of patient's molecules and thus Asclepiades could be viewed as introducing the modern concept of molecular stereopathology (Yapijakis, 2009).

By noting that differentiated types of human disease could arise in different ways and in different parts of the body, Asclepiades was postulating that this could be

based on the different sizes and shapes of the onkoi and the different sizes and shapes of the pores, that existed of different sites in the body. For example, the onkoi/pore relationship in the meninges of the brain, would be different to that of the relationship of the onkoi/pore relations that existed in the gastro-intestinal tract. Leith has recently said that this localization of pathological phenomena in specific parts of the body was fundamental to Asclepiades' approach to diagnosis and disease (Leith, 2020). This focus on the physical basis of disease within specific locations of the body was an early precursor to the more detailed understanding of pathology in modern medicine.

Most of Asclepiades' contributions to human disease causation were forgotten for about fifteen centuries. Then in the nineteenth century, John Dalton proved that the Atomic Theory was indeed a reality. In the twentieth century it was shown that all human diseases have a molecular basis, and the subsequent discovery of DNA provided a biochemical model of life at its first level of organization, initiating the era of molecular biology and molecular medicine (Porter, 1996; Runge et al, 2006; Yapijakis, 2009).

Yapijakis has said that Asclepiades of Bithynia should be viewed as the father of modern molecular medicine (Yapijakis, 2009).

Contribution to Modern Medical Classification

Asclepiades had a modern approach to medical classification. He was the first of the ancient physicians to arrange diseases into two main categories of acute and chronic (Yapijakis, 2009 and 2022). Freed from the misconception of the 'benevolent Nature' and influenced by the fourth Principal Doctrine of Epicurus regarding pains "those that are acute are more intense while those that are lasting are milder", Asclepiades recognized that some diseases have a short duration and the physician has to act swiftly in order to cure them, while other diseases are incurable and the best approach is to comfort the patients as much as possible (Yapijakis, 2009 and 2022). Asclepiades was saying that acute diseases were caused essentially by a constriction of the pores, or an obstruction of them by an excess of onkoi. Whereas chronic diseases were caused by relaxation of the pores, or a deficiency of the onkoi. However, it should be said that he

did separately mention that some milder clinical conditions occurred because of a disruption of the bodily fluids or of the pneuma. He also held that diseases do not end at a definite time, meaning that there were “no critical days” of any disease. While much of these farseeing ideas were lost for many centuries, his views on the classifications of acute and chronic diseases have endured to the present day.

Therapeutic Remedies

Asclepiades’ therapeutic remedies were essentially mechanistic. His recommended treatments should be aimed primarily at restoring harmony between the motion of the onkoi and the size of the apertures of the pores. As a physician Asclepiades was distinguished by the possession of personal qualities of compassion and kindness. His motto when treating his patients was to act: “swiftly, safely and pleasantly”. This approach was very modern in concept and was in stark contrast to the more aggressive and poorly thought-out of the many remedies of the time.

He was way ahead of his time, stressing the importance of convalescence and subsequent follow-up visits of his patients to their treating physician and emphasizing the great importance of the regular intake of a healthy diet and fresh water for adequate hydration.

Promotion of a Healthy Lifestyle and Good Dietetics

Asclepiades was a strong advocate of maintaining a healthy lifestyle. He promoted the taking of healthy foods to which should be ingested slowly and eaten on a regular daily basis. He also said that patients should only drink fresh water and to be aware of not eating stale food or drinking dirty water. He also stressed the importance of maintaining good personal hygiene and the role of moderate regular exercise. All of which was a very modern approach to healthy living.

Physical Therapy, Massage, Swinging Couches, Hydrotherapy

Cocchi (1788) refers to Asclepiades as suggesting that the various methods of exercising and restoring the body, which are universally used in the gymnastic art, are also useful in treating diseases (Cocchi, 1758 as quoted in Green, 1955).

Asclepiades advocated regulating controlled and supervised exercise as a significant component of his therapeutic regimes. He placed great emphasis on various forms of massage which would take place in well-lit rooms with ample fresh air. He designed special couches which would be suspended by ropes in a hammock-type arrangement that allowed patients to gently sway in a relaxing manner. These couches (“balnea pensilia”) could be modified for hydrotherapeutic techniques in a type of hypocaust arrangement which in most cases be followed by passive exercises (Benedum, 1967).

All the above recommendations are very similar to modern hydrotherapy and other therapies practices by professional physiotherapists.

Water Therapy

Asclepiades placed great emphasis on the role of fresh water as a therapy. As Yapijakis pointed out, Asclepiades was very much aware of how stagnant water in pools and rivers could cause disease (Yapijakis, 2009). Pliny refers to Asclepiades’ enthusiasm for cold water baths as a therapy (Pliny, NH.XXVI-3; Cocchi, in Green, 1955). However, he did not exclusively recommend cold water, as he often advised the use of warm water, either on its own, or in combination with cold water.

Drug Therapy, Purgatives and Enemas

At the time of Asclepiades’ medical practice in Rome, the use of a medley of various herbal and medicines (drugs) were being widely prescribed by the physicians of the time, as well as by the pater familia of the family households. Most of these herbal medications had significant adverse side effects as well as frequently being ineffective. Asclepiades was not opposed to the use of drugs as many scholars have suggested, however, he was one of the first of the ancient physicians to recognize the dangers of

their indiscriminate use (Scarborough, 1975). Pliny said that Asclepiades, not without cause, largely did away with the use of these (drugs) since almost all medications are evil juices and injure the stomach. He rather transferred all his own treatment to the regime of living itself (Pliny, H.N. XXVI.3.Cocchi, 1750 in Green, 1955).

Asclepiades was postulating that many of these herbal medications had no intrinsic powers of healing and according to his theory cures could be made in most case by restoring the balance between the onkoi and the pores, and in many cases, this could be achieved safely by giving the appropriate portions of food and wine (Gumpert, 1794 in Green, 1955).

Gumpert (1794) refers to the writings of Asclepiades in relation to his preparations where he quotes Asclepiades as having said that a physician who has compositions for each individual ailment, maybe for two or three, prepared and tested long before but being available for use when indicated (Gumpert, 1794 in Green, 1955).

Here we see Asclepiades referring to the importance of drug testing, centuries before modern strictly regulated drug trials have become the norm.

Asclepiades was extremely cautious about the use of purgatives and enemas which were being widely used by most physicians of the time in treating a wide and diverse number of clinical conditions. Although, it must be said that he recommended the use of certain purgatives and enemas to treat some clinical conditions.

He was particularly offended by the gluttonous custom of some wealthy Romans, who immediately after consuming a huge meal dinner, would undertake to eject their food by taking an emetic and subsequently vomiting, in order that they might then be able to ingest a greater amount of food (Green, 1955).

Venesection (Bloodletting)

Galen relates that Asclepiades employed venesection on occasions. Gumpert said that Asclepiades did not use venesection promiscuously but rather circumscribed it by certain suitable limits of doctrine that he taught (Gumper, 1794, in Green).

Caelius Aurelianus notes that Asclepiades, in keeping with other physicians of the time, was of the view that inflammation occurred in the body by the blood flowing

in an unnatural way to a specific part of the blood, where the blood (composed of large onkoi) would stagnate in the small veins, forming a painful swelling. Asclepiades took the view that in such inflammatory conditions, venesection was justified (Cael. Aurel., in Green, 1955).

Gymnastic Art

Gumpert has said that Asclepiades was the first of the Greek physicians practicing medicine in Rome who suggested that various methods of exercising and restoring the body was very useful in diseases (Gumpert, 1794 in Green, 1955).

Following on from earlier teachings of Herodicus of Trace, the fifth century BC so-called, “father of sports medicine”, Asclepiades was the first of the Greek physicians practicing the art in Rome, who was suggesting that individual physical exercises were useful in treating diseases of many different varieties (Green, 1955).

Genetics

Aristotle had believed that it was only males who contributed to the passing on of hereditary material to their progeny and that the female’s only role was to simply provide the proper bodily environment for the embryo to develop. However, two millennia before Gregor Mendel formulated the laws of genetics, which he had based on direct observational experiments, Epicurus was saying that human biological traits were inherited from both the male and the female. Epicureans were describing dominant, recessive, and co-dominant types of inheritance.

As a follower of Epicurus, it is reasonable to assume that Asclepiades would have taken a similar view (Yapijakis, 2017 and 2022).

Microbiology and Infectious Diseases

As documented by the Roman writer Terentius Varro, Asclepiades suggested that within stagnant waters invisible tiny animals (microbes) were living, and if inhaled or

ingested may cause diseases (Lindberg, 2007; Yapijakis, 2009). It was fifteen hundred years later, during the Renaissance that the Italian Girolamo Fracastoro wrote about minute living entities which he called “semina” as probably causing infection diseases (Nutton, 1990). With the invention of the medical microscope by the Dutchman Antoni van Leeuwenhoek in 1674, the existence of such living microorganisms was verified (van Zuylen, 1981). Later, Louis Pasteur’s experiments in 1875 proved that microbes acted as pathogens in causing human disease (Bordenave, 2003; Yapijakis, 2017).

Wine and its Medical Use

Asclepiades advocated the use of wine in moderation as an adjunctive to his treatment methods. He has been wrongly accused of liberally recommending the imbibement of wine just to please his patients, especially his wealthy ones. However, this is not true. He always recommended that the wine should be diluted with water, with the proportions of the wine and water depending on the type of disease being treated. For example, with heart conditions Asclepiades recommended that pure wine be given unmixed (Green, 1955, quoting Cael. Aurel morb ac [“acute”] II 39, p.176). Whereas in the case of catarrh, he recommended the mixing of one cup of wine with one cup of water (Green, 1955, quoting Cael. Aurel morb, ChR [“chronic”] II.7.p.386). He would also consider adding substances to the wine/water mix, such as honey, salt (brine wine), and barley (Gumpert, 1794, in Green, 1955).

Surgery

Asclepiades practiced to some extent as a surgeon (*chirurgii*), but only when he felt it was indicated to do so (Garzya and Marsullo, 2004). He has been credited with performing the first tracheostomy, which was possibly a cricothyroidotomy most likely performed for a tonsillar or pharyngeal obstruction, or possibly due to diphtheria (Gumpert, 1794; Frost, 1976; Yapijakis, 2009). Pliny, to his credit, does mention that Asclepiades refused to perform agonizing operations on the throats of sufferers with

quinsy, which reflects well on Asclepiades' moderate, restrained approach to patient's care (NH. 26.17).

Asclepiades also known to advise on occasions "scarification" of the lower limbs in cases of dropsy, painful peripheral oedema. He also wrote papers on the management of wounds, joint dislocations and on bone fractures (see p.14 of the thesis).

"Sayings" attributed to Asclepiades

- "Act Swiftly, Safely and Pleasantly."
- "Medical practice is not solely based on theories, but on experience combined with reason".
- "Healing is usually not only a matter of time, but sometimes a matter of opportunity."
- "He posited that bodily heat of the living human organism occurred as the result of the friction between the constantly moving onkoi, and not as the result of any "vital fire", that had been postulated earlier by Empedocles."
- "Everything occurs through necessity, and nothing occurs with a cause."

Overall, Asclepiades' contributions to modern medicine and surgery include the development of a new theoretical framework for understanding human disease, the challenge to prevailing medical doctrines, and the promotion of a more humane approach to patient care, particularly in the context of mental health.

5.1.2 Asclepiades and Modern Psychiatric Thought

During his lifetime as a practicing physician in Rome, Asclepiades gained a great reputation as a physician for his medical skills and especially for his humanistic and physiocratic approaches to his therapies. Asclepiades was an especially strong advocate for the mentally ill (Yapijakis, 2009). On his arrival in Rome to take up his medical practice, it was common for people who were considered to be insane to be locked up

in poorly lit, dark and damp confining spaces, which were essentially dungeons. They were frequently put in chain restraints or beaten and often deprived of adequate amounts of food and water (Gertz, 1994; Harris, 2013, Tzeferakos and Douzenis, 2014). When these so-called treatment methods failed to appease the gods, it was not unusual for these unfortunate very sick people to be put to death (Longrigg, 2013). Asclepiades strongly believed that this existing approach was not only inhumane, but it was totally wrong. His theory of disease causation made it obvious to him that as mental illnesses mainly occurred as the result of the impairment of onkoi in the brain area, then these barbaric approaches would only further misalign the patient's onkoi in the brain (Thumiger and Singer, 2018). His general therapeutic approach in treating patients with mental illnesses was essentially similar to his treatment approach to patients with other physical illnesses. He advocated that such patients should be released from their places of confinement, which must have been terrifying for them, so that they could be properly treated in the humane manner that he was suggesting. In keeping with his Epicurean philosophic approach, a characteristic saying of Asclepiades to his students and followers was that as long as there is friendship for man, there is also friendship for the medical art (Yapijakis, 2022). During the initial stages of mental illness, Asclepiades' somatic treatments included measures to build up the strength and constitution of the patient, with an emphasis on rest, gentle massage, relaxing fomentations, a restricted diet (initially), and limited venesection or bloodletting (on occasion). When the patient started to show signs of physical improvement, their treatment would gradually shift towards a normal diet, use of hot and cold baths (depending on the condition), as well as gentle, supervised physical exercise.

From a psychological perspective, the sickroom should be free of aggravating influences, including wall paintings that might excite the patient. Clinical management by trained servants (nurses) and physicians should deal sympathetically with the patient's hallucinations and delusions. Asclepiades recommended advocated psychotherapeutic measures stating that the treating sickroom should be free of any aggravating influences, such as some wall paintings that he felt might excite the patient. He stressed to his staff the importance that their clinical approach when managing their

patients should always be carried out sympathetically and in a compassionate manner. For example, he would advise the doctors and nurses when managing the utterances and sayings of hyperactive agitated patients should pretend to agree with them, in order to avoid over-exciting, them even further, but also when feasible, making corrections by pointing out the truth. However, he also advised that medical carers must be aware that certain clinical situations might demand the opposite approach and informing the patient of the true nature of their condition would then be the correct approach for their condition. Visiting was restricted, but occasionally a person whom the patient respected was brought into help overcome agitation and resistance, and to facilitate a calming atmosphere. Mental exercises such as reading, games, problem solving, and discussing written texts were encouraged at appropriate times and during lucid intervals, as was travel, for its relaxing effect. Witnessing drama performances was also recommended: mimes to counteract depression and tragedies to counteract hilarity (which was a term used in ancient times for the condition which is now described as elation or mania in the context of bipolar disorder).

Asclepiades particularly valued the role of music therapy in the general management of many illnesses, but this was especially so in the treatment of mental illness. He recommended different types of music depending on the nature of the case. For example, he suggested that music in the pleasant Phrygian mode would be prescribed for cases of depression, whereas music in the grave Dorian mode tradition could be employed in cases characterized childishness (Drabkin, 1955; Leon-Sanz, 2012). All the above approaches to therapy in mental illnesses are very much in keeping with modern psycho therapeutic methods.

In the second century AD the distinguished Roman philosopher and encyclopedist, Celsus proposed that there were three main types of mental illnesses: acute infections associated with fever (e.g., phrenitis), chronic mental illness without a fever (e.g., melancholia), and a particular chronic disorder that was generally characterized by mental confusion and hallucinations (Mudry,1993).Jackson has noted that the term “schizophrenia” was not used at that time (Jackson, 1986). Others have concluded that severe mental illness consistent with many of the clinical features of what is called schizophrenia today most probably existed in ancient Greece and Rome

(Kauffman and McLennan, 2017). Most of the other cases of aberrant behavior were believed to be caused by the wrath of the gods or demonic forces (Gazmuri, 2006).

Asclepiades and Phrenitis

The term phrenitis (aphrosyne) was first employed in ancient Greek medical thought by Hippocrates and his followers when it was referred to as “an affliction of the mind which was accompanied by an acute fever”. The presumed location of the condition within the human body was never anatomically or conceptually determined by the ancient physicians. The word phrenitis itself is derived from the Greek for diaphragm, which suggests that the condition might have been regarded as originating in the heart area. In keeping with Hippocratic thinking, phrenitis had been thought to be due to an excess of yellow bile within the humoral system in the body (Jackson, 1986).

Phrenitis was mentioned by Asclepiades and later by Soranos (98 AD-138 AD), whose work was recorded in the fifth century AD by Caelius Aurelianus (Drabkin, 1950). The concept of phrenitis persisted up to the nineteenth century, when it was largely replaced by delirium, a term that is currently accepted on being a serious disturbance in mental abilities that results in confused thinking and reduced awareness of the environment. Other contemporary terms for phrenitis included meningitis and encephalitis (Fredricks, 2011).

In his first book of his *De Morbis Acutis*, Caelius gives what he says is a quotation of the Asclepiadean definition of phrenitis as being a static obstruction or blockage of the onkoi in the cerebral membranes (meninges) which occur without any sympathetic affection, but with mental alienation and fever (Drabkin, 1950). Caelius was saying that Asclepiades’ theory on the etiology of phrenitis was that the cerebral membranes became heated due to the rapid movement of the onkoi as they moved towards the brain and the subsequent crowding of these onkoi on the brain membranes which then caused phrenitis. For more of Asclepiades’ views on phrenitis, it is necessary to look to Drabkin’s translation into English of Caelius’ Latin translation of Soranus’ *De Morbis Acutis et Chronicis* (“On Acute Diseases and on Chronic Diseases”), which was originally written in Greek. Caelius’ first book, *De Morbis*

Acutis. It is the best documented account of phrenitis in ancient literature. As a Methodist physician Caelius was however critical of what he felt were omissions by Asclepiades of what Caelius believed to be important physical symptoms of the condition. According to Caelius, Asclepiades erred in trying to explain the cause of phrenitis, rather than focusing on the signs and symptoms of the disease. This criticism of Asclepiades by Caelius is not surprising, as all Methodist physicians sought to know where the visible signs of a disease, rather than its causes (Vallance, 1990). Galen, in his treatise, “On Medical Experience”, did not refer to any of the physical clinical signs and treatment suggestions that Asclepiades had listed in his treatment recommendations for phrenitis, and just seemed to be more interested in attacking Asclepiades’ corpuscular theory.

The two sources which best explore Asclepiades’ recommended treatment of phrenitis are the writings of Caelius Aurelianus and of Antonio Cocchi. Asclepiades’ guiding principle in treating any acute medical condition such as phrenitis was that the physician had to act “safely, swiftly and pleasantly” (*cito, tutu, jucunde*) to best effect a cure. Asclepiades recommended that these patients should be placed in bright, aerated, well-lit rooms, and never in dark surroundings. Adequate hydration with tepid water was recommended twice daily. As diet was a very important component of Asclepiades’ treatment of phrenitis, he suggested providing easily digestible foods, in small amounts, three times daily. Pliny had said that Asclepiades always condemned the use of enemas in the treatment of phrenitis, but this was not the case. In fact, Asclepiades advised that enemas could be considered in certain cases, depending on the individual’s particular clinical situation. Asclepiades generally opposed purging, in keeping with his corpuscular theory. He also opposed bloodletting (venesection) in phrenitis, on the basis that the onkoi involved in phrenitis were very small, but plentiful, and would get obstructed in the interstices of the brain membranes and in the brain itself and venesection he argued, would lead to a deterioration in the condition.

In terms of the timing of treatment, Asclepiades believed that there were no “critical days” of diseases, meaning that illnesses did not end at a definitive time. He suggested that physicians should manage phrenitis in a carefully staged manner. On the first day, he recommended giving little food, but asking the patient to take plenty of

cold drinks. He suggested offering a choice of drinks to the patient, but no wine at this point. On the second day, if the fever persisted, he suggested that there should be no solid food intake, and fluid intake should be restricted to providing moderate amounts of cold water twice daily. The patient should be watched closely during this second night. By the third day he said that the condition of most patients would have started to improve. As their temperature started to fall, he encouraged increasing the soft solid foods intake. As their condition continued to improve, they could take more solid food suggesting by that, by the seventh day, the patient should be eating bread and fish, and taking small quantities of wine (Cocchi, 1758; Green, 1955).

What comes across is that Asclepiades was a very thoughtful, careful and caring physician, who would not take unnecessary risks with the management of patients with a serious medical condition such as phrenitis.

Asclepiades and Melancholia

The word melancholia, or melancholy, is derived from the Greek “melaena chole”, meaning black bile (Bell, 2014). According to Hippocrates and his followers, melancholia was due to an excess of black bile, which would then thicken and cause the condition (Stanley, 1983; Jackson, 1986; Berrios, 1996). In his *Aphorisms*, Hippocrates characterized melancholia as an affected mental disorder in which the clinical features of fear, sadness and despondency persisted for an extended period (Jones, 1923). Hippocrates also mentioned that melancholia could on occasions be associated with epilepsy.

When Asclepiades first arrived in Rome, it was common for the local physicians to administer a wide variety of herbal remedies in the treatment of mental afflictions, including melancholia. Such long-standing treatments for melancholia included shaving the patient’s head and then rubbing it with water infused with the verbena herb. Rose oil could also be poured over the head and into the nostrils. Some patients were advised to inhale another herb called rue with bitter-sweet plant solanum (a plant traditionally used to treat tuberculosis). The plant Muralis mixed with vinegar could also be rubbed into the head to alleviate delusions and sadness. Another form of

treatment was a scalp rub remedy using saffron mixed with the plant root orris. Concoctions of poppy or Hyoscyamus mixed with water were also recommended for “composing the mind”, while other doctors recommended smearing the forehead with cardamomum balsam or sycamine tears (Scarborough, 1969 and 1975).

Celsus specifically records Asclepiades as saying that herbal remedies for melancholia were of little or no use in the long term. Asclepiades was recommending an alternative approach to treatment of melancholia based in large part, but not exclusively, on his five main principles of therapy (Mudry, 1993).

In his monumental eight-book treatise *De Medicina*, Celsus wrote in a generally favorably way about Asclepiades and his treatments for melancholia. While Celsus was probably not a physician, he did say that Asclepiades by his concentration on dietetics and the healthy living regime, as opposed to pharmacology or surgery, had introduced an entirely new approach to Roman medicine (Mudry, 1993). Celsus also goes on to record that Asclepiades was saying that sufferers of melancholia would respond differently to being treated in either light or dark treatment rooms, with some patients preferring to be kept in dark rooms while others preferred to be treated in well-lit spaces. In that regard Asclepiades was arguing that the treatment of melancholia depended on the individual patient and the physician should be sensitive to their needs, adding: *Neutrum autem perpetuum est: alium enim lux, alium tenebrae magis turbent*, i.e., “Neither way is always right: light upsets some and darkness upsets others.”

Asclepiades’ overall management of mental illnesses was unsurprisingly modern in its approach. He showed remarkable awareness of the nuances of behavior by distinguishing the difference between delusions and hallucinations, and was also calling emotional disturbances, “passions of the sensations”. Asclepiades is considered by many physicians today as being the pioneer of the human approach to modern psychotherapy and psychiatry (Yapjakis, 2009). It can be seen from the above examples of two of the most common mental illnesses of his time, that Asclepiades was a very thoughtful, caring and farseeing physician in his assessment and treatment of patients with a variety of mental illnesses that occurred commonly at his time in Ancient Rome. By his own personal methods of medical practice and by his teachings

through the medical school that he had founded, Asclepiades' medical influence in the Graeco- Roman world lasted almost half a millennium.

5.1.3 *Asclepiades and Mental Illness*

Overall, Asclepiades' approach to mental illness was notably compassionate and thoughtful. He showed remarkable awareness of the nuances of behaviour, differences between delusions and hallucinations, and the idea of emotional disturbances as “passions of the sensations”. With considerable justification, Asclepiades is considered by many today as a pioneer of a more humane approach to psychotherapy and psychiatry (Yapijakis, 2009).

Asclepiades was not alone in urging a change of in attitudes towards apparent mental illness at this time. Elsewhere, Chinese medicine and Ayurvedic traditions, for example, offered different explanatory models for illness and various treatment approaches (Scull, 2015). Ayurveda held that disease resulted from imbalance of the doshas, or fluids in the body. Treatment depended on re-balancing these by a combination of medicines, diet, exercise, and rituals.

Asclepiades was especially interesting for his comprehensive application of his principles for the treatment of physical illness to mental illness, including diet, exercise, massage, bathing, and music. That was a remarkable step forward at that time. Through his medical school that he founded, and through his students and followers Asclepiades influence lasted almost half of a millennium. His ideas about mental illness set the scene for further evolution of attitudes towards the mentally ill and their treatment over subsequent centuries including, arguably, today.

5.1.4 *The Impact of Asclepiades' Ideas*

Perhaps the clearest echoes of Asclepiades' ideas about mental illness and its treatment is credible in the concept of “moral management” which emerged in the asylums of the

nineteenth century. In 1805, Jean-Etienne Dominique Esquirol (1772-1840), who was a French asylum doctor, was greatly influenced by the Epicurean Encyclopaedist, sensationalist and Catholic priest, de Condillac who defined moral management as “the application of the faculty of intelligence and of emotions in the treatment of mental alienation” (Esquirol, 1805; Brigham,1847). The moral management approach represented a significant from the immediate past which had emphasized custodial care rather than engagement with each patient as an individual.

Although its precise meaning was, at times rather vague, moral management had the key benefit of representing a significant, although by no means complete move away from interventions such as bloodletting, routine confinement and restraint, and a return to a more Asclepiadean approach to each patient as an individual.

Despite this promising idea, the apparently inexorable expansion of psychiatric institutions during the nineteenth and twentieth centuries saw the pendulum swing firmly away from the ideals of “moral management” and back towards institutional care (Kelly, 2016). A more Asclepiadean approach emerged again, However, in the later part of the twentieth century, as the asylums were gradually being dismantled and new approaches such as “milieu therapies” were starting to appear which involved a group-based approach to recovery with the establishment of therapeutic communities (Carlson and Dain,1960).

The more recent commitment to community-orientated care re-emphasizes core Asclepiadean values, as does the availability of occupational therapy, art and music therapies, although these areas clearly need further development in most places.

Many of the values that inform mental health care today, at least in theory, continue to echo Asclepiades approach, ranging from multi-disciplinary individual care-planning to programmes aimed at reducing restraints and coercion in psychiatric settings.

Contemporary iterations of these values tend to use the language of human rights, but the core moral ideas are highly consistent with Asclepiades’ views: treating each person as a unique human who needs treatment, care, and support in the least restrictive fashion possible.

As Asclepiades counselled, it remains the case that the physician should act “safely, swiftly, and pleasantly (*cito, tutu, jucunde*) to alleviate both physical and mental illness, whenever possible.

5.1.5 *Limitations of this Thesis*

Asclepiades of Bithynia was born about three centuries after Hippocrates and some two centuries before Galen. He was the first genuine Greek physician to have practiced and taught Greek medicine in Rome in the Golden Age of Cicero, Horace and Vergil. However, he remains a somewhat shadowy figure in ancient Roman medical history. Influenced by Epicurean philosophy, he sought to construct a new theory of human disease, derived in part from the atomic theories of chance and evolution described earlier by Democritus and Epicurus. Research into the life and times of Asclepiades has proved to be both difficult and challenging, as essentially none of his own writings have survived, apart from some broken fragments of his work. As a result, we must rely on some limited secondary work and the often-hostile testimony of later hostile writers, such as Pliny the Elder and Galen, whose views on Asclepiades are frequently inconsistent, spiteful, and often sarcastic.

This thesis is subject to several limitations. Firstly, none of Asclepiades’ writings survive today, apart from some fragments of his works within the works of other authorities.

As a result, ancient testimony relating to Asclepiades comes from some forty different authors (Cocchi, 1758). This means that access to his works is often indirect. This problem is not unique to Asclepiades as it is generally believed that Hippocrates did not write most of the treatises ascribed to him. As a result, most discussions of his work, and that of his follower are based on standard versions and translation of the Hippocratic canon (Jones, 1923).

Further limitation of this thesis is that the testimony of some later writers and their views on Asclepiades are frequently inconsistent and often opinionated. This author sought to compensate for these limitations by using multiple sources where

possible and placing the views of these other authors in their broader contexts. Even so, it would have been preferable to have more direct access to Asclepiades' work.

Finally, the secondary literature in this field is dispersed across both medical and historical literatures, making systematic literature searches challenging. This author sought to overcome this issue by searching for relevant papers in PubMed, Google Scholar, Brill, JSTOR, and the Loeb Classical Library, as well as general Internet searches. Relevant materials were identified and assembled, and further references listed as citations in these works were identified and pursued. Nevertheless, it remains the case that systematic literature searches in the field of medical history are challenging and often imperfect.

5.2 Future Directions

Based on research derived from the available extant material, this thesis has concluded that Asclepiades of Bithynia has made many contributions to modern medical practice, especially in the specialty areas of physiotherapy and psychiatry. His approach to both physical and mental illnesses was both reasoned and humane, and in many ways ahead of its time. He wrote extensively on a wide variety of mainly medical issues, as well as on some surgical topics. His written precepts on medical subjects, which are essentially all lost, apart from fragments, included such topics as: "Respiration", "About Pulses," "On Periodic Fevers," "On Dropsy," "On Enemas," "On Ulcers," "Safeguarding the Health," "The Duties of Doctors," "On Definitions," "Concerning Cardiac Lues," "Alopecia." (Green, 1955). Asclepiades was also interested in surgery and wrote precepts on wound healing and on the management of fractures and joint dislocations. He also has the distinction of being recognized as the first doctor to have performed a tracheostomy (Yapijakis,2009). Asclepiades belongs in the historical tradition of progressive approaches to the management of mental illness, not least because he applied his principles for the treatment of physical illness to mental illness. His ideas about psychiatry set the scene for further evolution of attitudes to mental illness and its treatment.

Interestingly, the book “Precepts”, which is included in the Hippocratic Corpus, contains so many of Asclepiades’ ideas that either he or one of his early students is probably the author (Yapijakis, 2009). The book contains references to acute and chronic diseases, diagnosis based on observation combined with reason and not theories, proper medical practice with sympathy, caring and friendliness toward patients, several Epicurean terms and views, as well as most importantly the Greek text contains Latinisms, indicating that the author spoke Latin and lived in Roman era (Yapijakis, 2009).

As none of Asclepiades’ own writings or copies remain, except for a few fragments, this presents huge problems for scholars of ancient Graeco-Roman history. While current Asclepiadean scholars will undoubtedly glean more important information from up-to-date expert analysis of the remaining extant fragments of Asclepiades’ works, recent significant scientific developments have taken place that may offer some hope in obtaining more historical information on the life and times of Asclepiades.

The volcanic eruption of Mount Vesuvius in 79 AD caused major destruction of the Roman city of Pompei which was situated near Naples in the Campania region of Italy. The associated pyroclastic lava flow from the volcano subsequently buried the adjacent wealthy Roman seaside town of Herculaneum up to 20 to 30 feet of volcanic ash and pumice (Barnes, 2011). Herculaneum was the summer retreat for many of the elite Roman ruling class, and archaeological excavations at the site of the buried city uncovered several splendid villas that contained exquisite ancient architecture that included large numbers of outstanding works of art, frescoes, bronzes and marble sculptures. Excavators subsequently uncovered a very large and elaborate Villa that contained an entire ancient library of over 1,800 neatly stacked carbonized hand-written scrolls of papyri, which had mainly Greek lettering but also some with Latin lettering. Most of the carbonized scrolls found to date are mainly copies of Epicurean philosophical texts, most of which cover Epicurus’ views on ethics, poetry, and music (Wallace-Hadrill, 2011). It is believed that this Villa, which became known as the *Villa dei Papyri*, was owned originally by the wealthy Roman senator Lucius Calpurnius Piso (101 BC-43 BC), who was the father-in-law of Julius Caesar. Piso was a friend of

the noted Epicurean philosopher and poet Philodemus of Gadara. Barker has speculated that Philodemus subsequently became the owner of the Villa, having previously lived there as a guest of Piso. Philodemus built up his large Epicurean library that was housed in this Villa (Barker,1908).

Philodemus was an Epicurean philosopher born in c110 BC Gadara situated in present day Umm Qais Jordan. Having studied in the Epicurean school in Athens, which at that time was led by Zeno of Sidon. He moved to Italy in the 70's BC and lived in Naples and perhaps also in Rome. He spent some time in Alexandria where he became friendly with Antiochus of Ascalon.

In the context of this thesis, the significance of the above is that Philodemus most likely knew Asclepiades or, at least, was near a contemporary of his when they both were at the Epicurean school in Athens around the same time, as well as later when they both lived in Rome. Asclepiades, like Philodemus, was greatly influenced by Zeno of Sidon when he was in Athens. Percy has speculated that as likeminded Epicurean intellectuals, both Asclepiades and Philodemus would have had many common academic interests (Percy, 2012). In a recent important article by Leith (2023) he refers to Lee Percy's paper (2012), where Percy was saying that Philodemus was "drawing on Asclepiades" medical theory, when he spoke about a type of particle in order to bolster his defense of Epicurus' psychology. All of the above gives an insight into the intellectual milieu that existed in Late Republican Rome (Leith, 2023).

The question that now arises as to whether it is reasonable to speculate that Philodemus, as a devoted follower of Epicurus and probably an intellectual friend of his fellow Epicurean Asclepiades, would have most likely included some of Asclepiades' written scrolls, or copies of same, in his Epicurean library in the Villa? This author takes the view that the above theory is a reasonable assumption to make at this time.

While the discovery of this great Library caused great excitement in the relevant academic circles, a big stumbling block presented itself to scholars when they tried to access the contents of these scrolls. This was due to the scrolls being sealed in carbonized volcanic ash and attempts to unroll them proved to be nearly impossible,

resulting in the breaking up of the brittle scrolls into very small fragments which generally were of little value to researchers. It should be noted that the Herculaneum scrolls have only survived for thousands of years because all the moisture had been seared out of the scrolls by the extreme superheat of the molten lava.

In 2013 two researchers, Brent Seales Professor of Computer Sciences in Kentucky University, and Daniel Delattre a distinguished French papyrologist, published a very important paper on the virtual unrolling of these carbonized scrolls (Seales and Delattre, 2013). While this was a significant development, a major problem remained in that the original Greek lettering and occasional Latin lettering, were not visually clear enough to allow accurate deciphering by the papyrologists. This was due in large part to their inability to be able to separate the carbon component of the original ink, from the trace carbon within the substance of the papyrus.

Further research by Seales and his scientific team in Kentucky led to a major breakthrough in solving this difficult problem, when the team developed a software machine learning algorithm, which was assisted by AI, that facilitated the increasing of the contrast between the carbon ink and the carbon-based papyrus. This breakthrough was achieved by utilizing medical-based x-ray phase contrast tomography which demonstrated that it is now possible to apply “virtual unwrapping” of the carbonized Herculaneum papyri scrolls. To date only about 8% of the estimated total of 1,800 scrolls have been virtually unwrapped (Parker and Seales, 2019).

The tantalizing prospect that perhaps some of the lost scrolls of the writings of Asclepiades are present within the library of the Villa, all neatly stacked and awaiting to be virtually unwrapped. At this point in time, we do not know if this will or will ever happen, or whether any of the remaining unwrapped scrolls contain any of Asclepiades’ lost works. But maybe, just maybe, some of Asclepiades’ lost work will emerge at some point in the future following their virtual unwrapping, more than two millennia after they had been sealed in volcanic carbonized ash, following the catastrophic eruption of Mount Vesuvius in 79 AD.

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Appendix A

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HISTORICAL AND LITERARY



Asclepiades of Bithynia: Greek physician and medical reformer

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Abstract

Asclepiades of Bithynia (124–40 BC) was a Greek physician who practised and taught Greek medicine in Rome. Among his many contributions, Asclepiades challenged the long-standing Hippocratic doctrine of the four humours. Influenced by Epicurean philosophy, he sought to construct a new theory of human disease, derived in part from atomic theories of chance and evolution earlier described by Democritus and Epicurus. In clinical practice, Asclepiades's approach to physical and mental illnesses was reasoned, humane, and, in many ways, ahead of its time. As a result of his many contributions and his overall approach to care, Asclepiades is now considered a pioneer of modern physical therapy, the progenitor of a more humane approach to mental illness, and, as highlighted by Yapijakis, the father of modern molecular medicine.

Keywords Asclepiades of Bithynia · Greek medicine · History of medicine · Mental illness · Molecular medicine · Tracheostomy

Asclepiades was born in 124 BC in Prusias-on-Sea in Bithynia, in the north-western region of present-day Turkey. Over the course of his eventful life, Asclepiades was recognised as one of the most original and influential figures at work in Rome during the period of the late Republic [1, 2]. Recent decades have seen increased interest in Asclepiades and his work, especially his prescient contributions to clinical medicine, many of which predated modern approaches by several centuries. This paper summarises Asclepiades's life and work, with particular emphasis on contributions and insights that are relevant to clinical practice today.

Little is known of Asclepiades's early life and none of his writings remains, except for fragments [3, 4]. He is arguably best known through the testimony of other, frequently less sympathetic ancient writers, such as Pliny the Elder (23–79 AD) and Galen (129–200 AD) [5–7]. Asclepiades is generally acknowledged by most scholars as being the physician to have firmly established Greek medicine in Rome [1].

Asclepiades arrived in Rome when he was about 30 years of age, at which time he was already an experienced physician [3]. It is generally agreed that Asclepiades initially taught rhetoric and philosophy, before commencing what was to prove a highly successful medical practice [1, 7–9].

Greek medicine in Rome

When Asclepiades first arrived in Rome, there was a significant climate of suspicion and hostility towards Greek doctors, generated in large part by Allbutt the Elder [10]. Asclepiades was not the first Greek doctor to arrive in Rome to start a medical practice — that dubious honour belongs to his fellow countryman, Archagathus. It is, however, generally agreed that Asclepiades was the first major authority on theoretical medicine to become established in Rome [1, 2, 11, 12].

Asclepiades boldly challenged the long-standing Hippocratic doctrine of the four humours, as well as its belief in the benevolence of nature [13, 14]. Influenced by Epicurean philosophy, Asclepiades sought to construct a new theory of human disease which was derived in part from the atomic theories of chance and evolution which had been earlier described by the philosophers Democritus (c460–c370 BC) and Epicurus (341–270 BC).

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Asclepiades theorised that the human body, like all other matter, was composed of theoretical atom-like particles called *önkoi*. These *önkoi* were not atoms in the strict sense of the word. Unlike traditional atoms, Asclepiades posited that these *önkoi* could divide into smaller fragments. Furthermore, *önkoi* had the potential to aggregate together in various shapes and sizes, called molecules. These molecules would move about in void space within the human body [7, 9, 15–18].

According to Asclepiades, health was maintained by the free and balanced motion of the *önkoi* passing through theoretical pores within the void spaces. Leith has called this system ‘void interstices’. Disease, on the other hand, was primarily the consequence of blockage or impaction of the *önkoi* in a particular part of the body. This specific localisation of pathological phenomena was fundamental to Asclepiades’s approach to diagnosis and treatment [9].

Asclepiades’s therapeutic remedies were essentially mechanistic, aimed primarily at restoring harmony between the motion of the *önkoi* and the size of the apertures of the pores within the void interstices. His most important therapeutic maxim in effecting a cure in an acute condition was for the physician to act safely, swiftly, and pleasantly: ‘ut tuto, ut celeriter, ut incudi curet’. In addition, he denounced the Hippocratic approach to chronic conditions, describing it as a ‘preparation for death’ [5].

Compassion and common sense

As a physician, Asclepiades was distinguished by two personal qualities: compassion and common sense. He avoided the drastic remedies that were fashionable among his contemporaries and immediate predecessors [2]. Unlike the followers of Hippocrates, it was only in extreme cases that Asclepiades recommended activities such as bloodletting, enemas, and purging, all of which were commonly used at the time [7, 15, 19].

Asclepiades was also the first physician to arrange diseases into the two main classes of acute and chronic. He suggested that acute diseases were essentially caused by either a constriction or an obstruction of the pores, or by an excess or altered shape of *önkoi*. Chronic diseases were caused by a relaxation of the pores or a deficiency of *önkoi* [20].

In acute medical conditions, Asclepiades advocated that the physician act swiftly in order to cure in a gentle and careful manner, whereas the best way to deal with incurable, chronic conditions was to comfort the patient in a humane manner and not subject them to rough or barbaric treatment [3, 5, 7, 21, 22].

Asclepiades’s approach to the practice of medicine was diametrically opposed to that of Archagathus, his infamous Greek predecessor who arrived in Rome in 219 BC and

practised medicine in a rough, barbaric manner. Asclepiades’s personality, careful manners, and gentleness helped him considerably to gradually overcome the Roman population’s general misgivings about Greek physicians [1, 2, 7].

Five principles of good health

In order to restore a patient to good health, Asclepiades advocated general therapies based on five key principles:

1. *Diet*. Asclepiades recommended regular intake of a diet of healthy food, fresh water, and, in some instances, moderate amounts of wine [1, 7, 20];
2. *Exercise*. Asclepiades suggested light but strictly regular physical exercise, which could be supervised by a doctor for patients who were unable to exercise independently. Such activities included exercises on swinging/swaying ‘hanging baths’ which Asclepiades had designed (‘*balnea pensilia*’) and which could be modified for hydrotherapeutic techniques [23];
3. *Massage*. Asclepiades placed great emphasis on gentle massage in well-lit rooms in congenial surroundings with ample fresh air;
4. *Bathing*. Asclepiades recommended regular bathing in cold or warm water, depending on the specific clinical condition, accompanied by gentle, passive exercises; and
5. *Music*. Asclepiades suggested use of selected forms of music for certain conditions, such as depression.

In addition to this advice, Asclepiades held that many ancient medical drugs and herbs were bad for the stomach. He said that drugs ought not to be given to patients with fevers or acute illnesses, suggesting carefully regulated food and wine instead. He was not completely opposed to the prescription of drugs, as some scholars have suggested, but restricted their use to very specific conditions [24]. Indeed, Asclepiades was frequently referred to as ‘*pharmicon*’, owing to his detailed knowledge of medical herbs [7, 25].

Across all of his medical therapies, Asclepiades advocated that the physician should pay as much attention to the convalescence of the recovering patient as to the immediate treatment of the illness. In this regard, Asclepiades appears to have been a reasonable, prudent doctor who was well received by his patients, especially his wealthy ones [20]. He was ahead of his time in many ways [22, 26].

Surgery, mental illness, and music therapy

In addition to his medical treatments, Asclepiades practised as a surgeon (‘*chirurgii*’), but only when he felt it was indicated to do so [27]. The ancient medical writers Galen and

Aretaeus, both of whom lived in the second century AD, credit Asclepiades with performing the first tracheostomy. This was probably a cricothyroidotomy, most likely for a pharyngeal obstruction, possibly due to diphtheria [3, 6, 7]. Asclepiades was, however, selective in his surgical practice: Pliny mentions that Asclepiades refused to perform agonising operations on the throats of sufferers with quinsy [28].

Asclepiades was also a strong advocate for the mentally ill, making extensive studies of mental illness and clearly differentiating between hallucinations and delusions [29]. His theory of disease mechanisms made it clear to him that mental disease occurred as the result of impaired *önkoi* in the brain [30].

Asclepiades's therapeutic approach to mental illness was essentially similar to his treatment of physical illnesses. At that time in Rome, it was common for people who were considered 'insane' to be locked in dark confining places which were essentially dungeons [31]. Asclepiades believed that this approach further misaligned the brain *önkoi*. He advocated that patients with mental illness should be released from these places of terrifying confinement so that they could be properly treated in the manner he suggested.

Asclepiades's primary therapeutic aim was to provide a comfortable setting for people with mental illness so that his natural regimens of therapy could be provided safely and sympathetically, thus facilitating harmony between the *önkoi* and the pores in brain. He strongly recommended music therapy, and while he was not the first to suggest this technique, his approach stood in stark contrast to the generally barbaric treatment of mental illness in Rome at that time [32].

Conclusions

Overall, Asclepiades's treatments were often surprisingly modern in their approach to physical and mental illnesses. As a result, this neglected Greek physician is now considered by many medical historians as a pioneer of modern physical therapy, the progenitor of a more humane approach to mental illness, and, as highlighted by Yapijakis, the father of modern molecular medicine [7]. Asclepiades's life and work merit closer attention than they have received to date, and many of his insights bear reflection and application today, some two millennia after he first expounded them.

Declarations

Ethics approval This was an historical study based on publicly available documents that did not require ethical review. This paper is in accordance with the ethical standards of the institutional and national research committees, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Conflict of interest The authors declare no competing interests.

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Historical Paper

Greek physician Asclepiades of Bithynia (124–40 BC) and his contribution to thinking about mental illness and its treatment

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Abstract

Objectives: To outline the life and work of Greek physician Asclepiades of Bithynia (124–40 BC), especially his contributions to thinking about mental illness.

Methods: Review and discussion of relevant fragments of Asclepiades' work that survive and review of secondary literature, supplemented by relevant systematic literature searches (e.g. PubMed).

Results: Asclepiades challenged the long-standing Hippocratic doctrine of the four humours and developed an approach to physical and mental illness that was humane, reasoned, and a forerunner of later developments in psychiatry. Asclepiades argued that the human body, like everything in the universe, comprised tiny, imperceptible particles, which he called *ōnkoī*, seamless masses in perpetual motion. In consequence, Yapijakis describes Asclepiades as 'the father of molecular medicine'. Asclepiades held that good health was maintained by free, balanced motion of *ōnkoī* through theoretical pores, while disease resulted from blockage or impaction of *ōnkoī* passing through pores in various body parts (e.g. brain). Based on this idea, Asclepiades recommended releasing people with apparent mental illness from confinement and using judicious combinations of diet, exercise, massage, bathing, and music to treat 'phrenitis' (delirium) and melancholia. He suggested that the physician act 'safely, swiftly and pleasantly' ('cito, tutu, jucunde') for both physical and mental illness.

Conclusions: Asclepiades belongs to the historical tradition of progressive medical approaches to mental illness, not least because he applied his principles for the treatment of physical illness to mental illness. His ideas about psychiatry set the scene for further evolution of attitudes to mental illness and its treatment over subsequent centuries.

Keywords: Asclepiades of Bithynia; Greek medicine; History of psychiatry; Mental illness; Molecular medicine; Treatment

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Introduction

Asclepiades of Bithynia (124–40 BC) was a Greek physician who practised and taught Greek medicine in Rome and made particular contributions to the understanding of mental illness at that time. Influenced by Epicurean philosophy, Asclepiades sought to construct a new theory of human disease, derived in part from atomic theories of chance and evolution earlier described by Democritus and Epicurus (Brady and Kelly 2023). Asclepiades challenged the long-standing Hippocratic doctrine of the four humours and developed an approach to physical and mental illnesses that was humane, reasoned, and, in certain ways, a forerunner of many subsequent developments in medicine and psychiatry. Yapijakis accurately describes Asclepiades as 'the father of molecular medicine' (Yapijakis 2009; Yapijakis 2017).

We have previously published a paper primarily examining Asclepiades' contribution to the understanding and treatment of

physical illnesses, among other matters (Brady and Kelly 2023). By contrast, the current paper focuses on Asclepiades' contribution to thinking about mental illness and its treatment. The paper starts by presenting an introduction to Asclepiades' life and work; outlines the paper's methodology; summarises Asclepiades' contribution to psychiatric thought; presents his particular views on 'phrenitis' (or delirium), melancholia, and their treatment; and draws relevant conclusions about Asclepiades' work and overall contribution to thinking about mental illness and its treatment.

Background to Asclepiades of Bithynia

Asclepiades was a Greek physician who practised and taught Greek medicine in Rome (Raynaud 1862; Wellman, 1908; Wellman, 1929; Rawson 1982; Polito 1999; Flemming 2012). Born in 124 BC in Prusias-on-Sea in Bithynia (the north-western region of present-day Turkey), Asclepiades is generally accepted by most scholars as being the first leading representative of Greek theoretical medicine to work as a practising physician in Rome.

When Asclepiades first arrived in Rome, his knowledge of medicine and philosophy, coupled with his considerable rhetorical skills and personality, allowed him not only to flourish as a

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physician but to be accepted into the intellectual and sophisticated aristocratic circles that existed in Rome during the late Republican period. Asclepiades boldly challenged the long-standing Hippocratic doctrine of the four bodily humours, as well as its 'benevolent nature' axiom.

Asclepiades held that a fully-fledged theory of matter was necessary for the understanding and practice of medicine and posited an innovative systematic medical theory that drew extensively on Epicurean atomism. Asclepiades argued that the human body, like everything else in the universe, was composed of tiny, imperceptible particles, which he called *ōnkoi*. According to his theory, these seamless masses were in perpetual motion, bouncing around forever within a void space, without having any providential intelligence at work in the universe to guide them. For more on this theme, see Leith (2009) and Leith (2012).

Asclepiades postulated that the *ōnkoi* were of different shapes and sizes, lacked colour and sensitivity, and possessed the capacity to aggregate together by chance to form larger masses that ultimately formed all of the components of the universe, including the human body. Unlike the indivisible atoms of Epicurus, Asclepiades held that these *ōnkoi* were capable of splitting into innumerable smaller fragments which could then move around in the void space.

In terms of medicine, Asclepiades created a theory that held that good health was maintained by the free and balanced motion of the *ōnkoi* through theoretical pores within the void space, while disease was the consequence of blockage or impaction of the *ōnkoi* passing through the pores at a particular part of the human body. Specific diseases resulted from blockages at different sites. Against this theoretical background, Asclepiades' practical approach to the management of physical and mental illnesses was reasoned and humane. In consequence, he is now considered a pioneer of modern physical therapy and the progenitor of a more humane approach to mental illness (see below).

Methodology

The methods of medical history differ from research methodologies in other areas of medicine (Burnham 2005). Systematic literature searches, common in other areas of medical research, are often insufficient for the medical historical literature. While systematic searches are helpful in identifying a certain portion of the recent academic literature, they need to be supplemented by interrogation of other historical sources, standard translations of particular works, and – where available – ancient texts. This multimodal approach is especially necessary in the case of Asclepiades.

Despite his historical significance, Asclepiades remains a relatively obscure figure in ancient medical history. None of his writings have survived apart from some fragments of his works in the works of other authorities. As a result, ancient testimony relating to Asclepiades comes from some 40 different authors (Cocchi 1758). In consequence, it is necessary to rely on the testimony of these later writers, whose views on Asclepiades are frequently inconsistent and often opinionated. This is especially true in the case of Pliny the Elder (23–79 AD) and, later, Galen (129–200 AD) (Galen; transl. Brock, 1916). Against this background, the current paper is based on literature searches relevant to the paper's theme, consideration of the secondary literature, and review of relevant fragments of Asclepiades' work that survive (e.g. King 2001; Thumiger and Singer 2018).

For the literature searches, pertinent keywords ('Asclepiades', 'Ancient Roman medicine') were used to search for papers in

PubMed, Google Scholar, Brill, JSTOR, and the Loeb Classical Library, as well as general Internet searches. Relevant materials were identified and assembled, and further references listed as citations in these works were identified and pursued. Key ancient texts from this overview of the historical literature include *Discorso Primo Sopra Asclepiade* (Cocchi 1758), *On Acute Diseases and On Chronic Diseases* (Caelius Aurelianus; transl., Drabkin, 1950), and *On the Natural Faculties* (Galen; transl. Brock, 1916). These source materials are discussed in this paper.

Other ancient sources are not available in a primary format and are discussed in our paper based on secondary sources, as is customary in this literature. For example, it is believed that Hippocrates did not write any treatises, so we discuss the work of Hippocrates' followers based on a standard version and translation of the Hippocratic canon, that is, *Hippocrates: An English Translation* (Jones 1923).

Results

Asclepiades and psychiatric thought

In the second century AD, Celsus (a Greek philosopher; 25 BC–50 AD) proposed that there were three main types of mental illnesses: acute affections associated with fever (e.g. 'phrenitis'), chronic mental illness without fever (e.g. melancholia), and a particular chronic disorder that was generally characterised by mental confusion and hallucinations (although the term 'schizophrenia' was not used at that time) (Jackson 1986). Most of the other cases of aberrant behaviour were believed to be caused by the wrath of the gods or demonic forces (Gazmuri 2006).

Against this background, Asclepiades, as a practising physician in Rome, gained a considerable reputation as a physician for both his medical skills and his humane approach to treating physical and mental illness. Asclepiades was an especially strong advocate for the mentally ill (Yapjakis 2009). On his arrival in Rome to take up his medical practice, it was common for people who were considered to be insane to be locked in poorly lit, dark, and damp confining spaces, which were essentially dungeons. They were frequently placed in chain restraints or beaten, and often deprived of adequate food and water (Gerdtz 1994; Harris, 2013; Tzeferakos and Douzenis 2014). When these so-called treatment methods failed to appease the gods, it was not unusual for them to be put to death (Longrigg 2013).

Asclepiades believed that this approach was not only inhumane but medically wrong. His theory of disease causation made it obvious to him that mental illness occurred as the result of impaired *ōnkoi* in the brain, and barbaric approaches would only further misalign the *ōnkoi* in the brain (Thumiger and Singer 2018). As a result, Asclepiades' therapeutic approach to mental illness was essentially similar to his approach to physical illness.

First, Asclepiades advocated that patients should be released from their places of confinement so that they could be properly treated in the manner he suggested. During the initial stages of mental illness, Asclepiades' somatic treatments included measures to build up the strength and constitution of the patient, with an emphasis on rest, gentle massage, relaxing fomentations, a restricted diet (initially), and limited venesection or bloodletting (on occasion). He generally opposed the use of emetics and purgatives at this stage. When the patient showed signs of physical improvement, their treatment would gradually shift towards a normal diet, use of hot and cold baths (depending on the condition), and gentle, supervised physical exercise.

From a psychological perspective, Asclepiades recommended that the sickroom should be free of aggravating influences, including wall paintings that might excite the patient. Clinical management by trained servants (nurses) and physicians should deal sympathetically with the patient's hallucinations and delusions. This meant pretending to agree with them at times, in order to avoid over-exciting the patient, but also, when feasible, making corrections by pointing out the truth. Visiting was restricted, but occasionally a person whom the patient respected was brought in to help overcome agitation and resistance and to facilitate a calming atmosphere. Mental exercises such as reading, games, problem-solving, and discussing written texts were encouraged at appropriate times and during lucid intervals, as was travel, for its relaxing effect.

Witnessing drama performances was also recommended: mimes to counteract depression and tragedies to counteract hilarity (which was a term used for the condition which is now described as elation or mania in the context of bipolar disorder). Asclepiades particularly valued the use of music in the treatment of mental illness. He recommended different types of music depending on the nature of the case. For example, he suggested music in the pleasant Phrygian mode for depression, and music in the grave Dorian mode for cases characterised by childishness (Drabkin 1955; León-Sanz 2012).

Asclepiades, phrenitis, and delirium

The term 'phrenitis' or phrenosis was first employed in ancient Greek medical thought by Hippocrates and his followers. It was referred to as an affliction of the mind which was accompanied by an acute fever. The presumed location of the condition within the human body was never anatomically or conceptually determined. The word 'phrenitis' itself is derived from the Greek for 'diaphragm', which suggests that the condition might have been regarded as originating in the heart area. In keeping with Hippocratic thinking, phrenitis had also been attributed to an excess of yellow bile within the humoral system of the body (Jackson 1986).

The term phrenitis was mentioned by Asclepiades and later by Soranus (98–138AD), a Greek physician whose work was recorded in the fifth century AD by Caelius Aurelianus (1950). The concept of 'phrenitis' persisted up to the 19th century, when it was largely replaced by 'delirium', a term denoting a transient and fluctuating disturbance in mental abilities that results in confused thinking and reduced awareness of the environment, often owing to an identifiable physical cause (such as infection).

In his first book of his 'De Morbis Acutis', Caelius provided the Asclepiadean definition of phrenitis as 'static obstruction or blockage of the corpuscles (*ōnkoi*) in the cerebral membranes (meninges) which occurs frequently and without any sympathetic affection, but with mental alienation and fever' (Caelius Aurelianus, 1950). Caelius argued that Asclepiades' theory on the aetiology of phrenitis was that the cerebral membranes became heated due to the rapid movement of the *ōnkoi* as they moved towards the brain and the subsequent crowding of the *ōnkoi* on the brain membranes caused phrenitis.

For more of Asclepiades' views on phrenitis, it is necessary to look to Drabkin's translation into English of Caelius' Latin translation of Soranus' 'De Morbis Acutis et Chronicis' ('On Acute Diseases and on Chronic Diseases'), which was originally written in Greek (Caelius Aurelianus, 1950). Caelius' first book,

'De Morbis Acutis', is the best-documented account of phrenitis in the ancient literature. As a Methodist physician, Caelius was critical of what he felt were omissions by Asclepiades of what Caelius believed were important physical symptoms of the condition. According to Caelius, Asclepiades erred in trying to explain the cause of phrenitis, rather than focusing more on the signs and symptoms of the disorder.

This criticism of Asclepiades by Caelius is not surprising because Methodist physicians focused primarily on the visible signs of a disease, rather than its causes (Vallance 1990). Galen, in his treatise 'On Medical Experience', gave a different account of Asclepiades' management of phrenitis and, compared to Caelius, was more interested in attacking Asclepiades' corpuscular theory, rather than clinical details. In addition, Galen did not mention any of the signs of phrenitis which Asclepiades had mentioned and which were described and attributed to Asclepiades in Caelius' text.

Asclepiades' guiding principle in treating any acute medical condition such as phrenitis was that the physician had to act 'safely, swiftly and pleasantly' ('cito, tutu, jucunde'). Patients should be placed in bright, aerated, well-lit rooms, and never in dark surroundings. Adequate hydration with tepid water was recommended twice daily. As diet was a very important component of treatment, Asclepiades recommended easily digestible foods, in small amounts, three times daily.

Pliny said that Asclepiades condemned the use of enemas in the treatment of phrenitis, but this was not the case. In fact, Asclepiades advised that enemas could be considered in certain cases, depending on the individual's clinical situation. Asclepiades opposed purging, in keeping with his corpuscular theory. He also generally opposed bloodletting (venesection) in phrenitis, on the basis that the *ōnkoi* involved in phrenitis was very small, but plentiful, and would get obstructed in the interstices of the brain membranes and in the brain itself. Venesection, he argued, would lead to a deterioration in this condition.

In terms of the timing of treatment, Asclepiades believed that there were no 'critical days' of diseases, meaning that illnesses did not end at a definitive time. With this in mind, he suggested that physicians should manage phrenitis in a carefully staged manner. On the first day, he recommended giving little food but asking the patient to take plenty of cold drinks. He suggested offering a choice of drinks to the patient, but no wine at this point. On the second day, if the fever persisted, he suggested that there should be no solid food intake and fluid should be restricted. It was appropriate to provide moderate amounts of cold water twice daily. The patient should be watched closely during the second night.

By the third day, most patients would have started to improve, he believed. As their temperature started to fall, he encouraged soft solid foods. As they continued to recover, they could take more solid food, and by the seventh day, the patient should be eating bread and fish and taking small quantities of wine (Cocchi 1758; Green 1955). Overall, Asclepiades comes across as a thoughtful, careful physician, who would not take unnecessary risks with the management of patients with a serious medical condition such as phrenitis.

Asclepiades and melancholia

The word melancholia, or melancholy, is derived from the Greek 'melaena chole', meaning black bile (Bell 2014, p. 38). According to Hippocrates and his followers, melancholia was due to an excess of black bile, which would thicken and cause the

condition (Jackson 1983; Jackson 1986; Berrios 1996). In his 'Aphorisms', Hippocrates characterised melancholia as a mental disorder in which the clinical features of fear, sadness, and despondency persisted for an extended period of time (Jones 1923). Hippocrates held that melancholia could be associated with epilepsy on occasion.

When Asclepiades first arrived in Rome, it was common for the local physicians to administer a wide variety of herbal remedies in the treatment of mental afflictions, including melancholia. Such treatments included shaving the patient's head and then rubbing it with water infused with verbenae (a herb). Rose oil could also be poured over the head and into the nostrils. Some patients were advised to inhale rue (a herb) with bitter-sweet solanum (a plant traditionally used to treat tuberculosis).

Muralis (another plant), mixed with vinegar, could be rubbed into the head to alleviate delusions and sadness. Another form of treatment was a scalp rub remedy using saffron mixed with orris (root). Concoctions of poppy or hyoscyamus (papaver aut hyoscyamos) mixed with water were recommended for 'composing the mind', while other doctors suggested smearing the forehead with cardamomum balsam or sycamine tears (Scarborough 1969; Scarborough 1975).

Not all physicians agreed with this approach to melancholia. Celsus specifically records Asclepiades as saying that herbal remedies had no long-term benefit in melancholia. Asclepiades recommended an alternative approach based in large part on his five main principles of therapy: diet, exercise, massage, bathing, and music.

In his monumental eight-book treatise 'De Medicina', Celsus wrote generally favourably about Asclepiades and his treatments for melancholia. While Celsus was a distinguished Roman encyclopaedist, it is unclear if he was a physician. Nonetheless, he says of Asclepiades that 'by his concentration on dietetics, the healthy regime, as opposed to pharmacology or surgery, Asclepiades had introduced an entirely new epoch to Roman medicine' (Mudry 1993).

Celsus goes on to record Asclepiades saying that 'sufferers of melancholia respond differently to light or dark rooms with some preferring to be kept in dark rooms while others prefer well-lit spaces'. In that regard, Asclepiades argued that treatment depended on the individual patient and the physician should be sensitive to their needs, adding that 'neutrum autem perpetuum est: alium enim lux, alium tenebrae magis turbent' (i.e. 'neither way is always right: light upsets some and darkness upsets others').

Discussion

Summary of main findings

Asclepiades challenged the long-standing Hippocratic doctrine of the four humours and developed an approach to physical and mental illness that was humane, reasoned, and a forerunner of later developments in psychiatry. He held that the human body, like everything in the universe, comprised tiny, imperceptible particles, which he called *ōnkoi*, seamless masses in perpetual motion. Asclepiades believed that good health was maintained by free, balanced motion of *ōnkoi* through theoretical pores, while disease resulted from blockage or impaction of *ōnkoi* passing through pores in various parts of the body (e.g. the brain).

Based on this idea, Asclepiades recommended releasing people with apparent mental illness from confinement and using judicious

combinations of diet, exercise, massage, bathing, and music to treat 'phrenitis' (delirium) and melancholia. One of Asclepiades' greatest contributions was the fundamental idea that physicians should approach mental illness in a fashion that was similar to how they approached physical illness.

Limitations of this paper

This paper is subject to a number of limitations. First, none of Asclepiades' writings survive today, apart from some fragments of his works within the works of other authorities. As a result, ancient testimony relating to Asclepiades comes from some 40 different authors (Cocchi 1758). This means that access to his works is often indirect. This problem is not unique to Asclepiades: it is believed that Hippocrates did not write any treatises, so most discussions of his work, and that of his followers, are based on standard versions and translations of the Hippocratic canon, for example, *Hippocrates: An English Translation* (Jones 1923).

It is a further limitation of our paper that the testimony of these later writers and their views on Asclepiades are frequently inconsistent and often opinionated. We sought to compensate for these limitations by using multiple sources where possible and placing the views of other authors in their broader contexts. Even so, it would be preferable to have more direct access to Asclepiades' work.

Finally, the secondary literature in this field is dispersed across both the medical and historical literatures, making systematic literature searches challenging. We sought to overcome this issue by searching for relevant papers in PubMed, Google Scholar, Brill, JSTOR, and the Loeb Classical Library, as well as general Internet searches. Relevant materials were identified and assembled, and further references listed as citations in these works were identified and pursued. Nevertheless, it remains the case that systematic literature searches in the field of medical history are challenging and often imperfect.

Asclepiades and mental illness

Overall, Asclepiades' approach to mental illness was notably compassionate and thoughtful. He showed remarkable awareness of the nuances of behaviour, differences between delusions and hallucinations, and the idea of emotional disturbances as 'passions of the sensations'. With considerable justification, Asclepiades is considered by many today as a pioneer of a more humane approach to psychotherapy and psychiatry (Yapjakis 2009).

Asclepiades was not alone in urging a change in attitudes towards apparent mental illness around this time. Elsewhere, Chinese medicine and Ayurvedic traditions, for example, offered different explanatory models for illness and various treatment approaches (Scull 2015; p. 46). Ayurveda held that disease resulted from an imbalance of the *doshas*, or fluids in the body. Treatment depended on re-balancing these with a combination of medicines, diet, exercise, and rituals.

Asclepiades was especially interesting for the comprehensive application of his principles for the treatment of physical illness to mental illness, including diet, exercise, massage, bathing, and music. That, in itself, was a remarkable step forward at that time. Through the medical sect he founded and through his students and followers, Asclepiades' influence lasted almost half a millennium. His ideas about mental illness set the scene for further evolution of attitudes towards the mentally ill and their treatment over subsequent centuries including, arguably, today.

The impact of Asclepiades' ideas

Perhaps the clearest echoes of Asclepiades' ideas about mental illness and its treatment are discernible in the concept of 'moral management', which emerged in the asylums of the 19th century. In 1805, Jean-Étienne Dominique Esquirol (1772–1840), a French asylum doctor, defined moral management as 'the application of the faculty of intelligence and of emotions in the treatment of mental alienation' (Esquirol 1805; Brigham 1847). The moral management approach represented a significant break from the immediate past that had emphasised custodial care rather than engagement with each patient as an individual. Although its precise meaning was, at times, rather vague, moral management had the key benefit of representing a significant (although by no means complete) move away from interventions such as bloodletting, routine confinement, and restraint and a return to a more Asclepiadean approach to each patient as an individual.

Despite this promising idea, the apparently inexorable expansion of psychiatric institutions during the nineteenth and twentieth centuries saw the pendulum swing firmly away from the ideals of 'moral management' and back towards institutional care (Kelly 2016). A more Asclepiadean approach emerged again, however, in the latter part of the 20th century, as the asylums were gradually dismantled and approaches such as 'milieu therapy' appeared, involving a group-based approach to recovery and establishment of therapeutic communities (Carlson and Dain 1960). The more recent commitment to community-oriented care re-emphasises core Asclepiadean values, as does the availability of occupational therapy, art, and music therapies in inpatient centres, although these areas clearly still need further development in most places.

Today, many of the values that inform mental health care, at least in theory, continue to echo Asclepiades' approach, ranging from multi-disciplinary individual care planning to programmes aimed at reducing restraints and coercion in psychiatric settings. Contemporary iterations of these values tend to use the language of human rights, but the core moral ideas are highly consistent with Asclepiades' views: treating each person as a unique human who needs treatment, care, and support in the least restrictive fashion possible. As Asclepiades counselled, it remains the case that the physician should act 'safely, swiftly and pleasantly' ('cito, tutu, jucunde') to alleviate both physical and mental illness, whenever possible.

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