

CHAPTER 1 FRENZY & STUPOR

In lectures, articles or textbooks tackling bipolar disorder, or manic-depressive illness, distinguished professors of psychiatry and other academics repeatedly, indeed almost universally, start by claiming the Greeks and Romans recognized this disorder¹. But while the terms mania, melancholia, insanity, dysphoria, dysthymia, paranoia, frenzy and lunacy all go back to the Greeks and Romans, manic depressive disease does not and indeed could not.

Ten years ago, it might have been possible to write off two thousand years of history and start instead at the end of the 19th century when the German psychiatrist, Emil Kraepelin, established manic-depressive illness in its modern form². From 1899, even though the illness is more likely to be called bipolar disorder now, we have a history that can be researched as solidly as anything in biological psychiatry. Claims about events from the end of the 19th century onward can be supported by solid banks of evidence or challenged by an appeal to other evidence. It should be possible to establish areas of consensus about the history of mood disorders and move on to collect evidence on areas of continuing uncertainty just as science itself does.

But the launch of mood-stabilizing drugs for bipolar disorder in the mid 1990s means that we cannot write off these two thousand years, because since then contemporary biological psychiatrists have invoked the past repeatedly. Their invocations suggest that modern manic-depressive illness is not set on solid ground and claiming Greek precedents stems from a hope that the antiquity of such authorities will confer legitimacy on contemporary therapeutic and research endeavors. Almost every artist, composer, or author of note in the 18th and 19th centuries, as we shall see in chapter 5, has been similarly invoked as prior sufferers from this illness.

If my argument that the disease was not and could not have been recognized before the 19th century is right, then this is a case of the present colonizing the past. If present powers seek to rewrite the past in this way, we need to see whether the edifice of manic-depressive illness we are faced with today is quite as stable if the props marked "history" are knocked out from under it.

But there are further reasons for not ignoring the past. The first is that this book is not just a history of one disease. It is also about how we understand ourselves, about how we fit ourselves into our bodies, or fit our minds into our

¹ Goodwin F K, Jamison KR (1990). *Manic Depressive Illness*. Oxford University Press, New York; Angst J, Marneros A (2001). Bipolarity from ancient to modern times: conception, birth and rebirth. *Journal of Affective Disorders* 67, 3-19; See Nordic Psychiatry Academy, Jan 20th 2006 http://gdp.videoarkiv.net/janssen-cilag/20012006_JC_DK_nordic_academy/default.html, accessed March 28th 2006.

² Kraepelin E (1899). *Psychiatrie. Ein Lehrbuch für Studierende und Aertze*. 6th Edition. Leipzig, JA Barth, translated JM Quen, Watson Publishing, Canton USA.

brains. We have had great difficulties in embodying the mind and in understanding how a “mind” can be diseased and these difficulties played a key role in blocking recognition of manic-depressive disorder. If this is the case, then conversely current conceptions of this disorder, and perhaps this disorder more than any other, and the embodiment such conceptions imply, must have implications for how we understand ourselves now.

Second, the difficulties in establishing the existence of a mood disorder tell us something about how clinicians make diagnoses. For the Greeks, this was by visible signs that made it reasonable to locate the problem in the body of the sick person. For us, diagnoses depend on what people say. We have moved as a result into a world in which illnesses are negotiated, the consequences of which will be with us through the book. We have moved into a world in which in the absence of visible pathology we have no way of being certain whether the individual is sick rather than society.

The third issue is that whatever about whether a disease entity was recognized before the 19th century, “dis-ease” has provided a living for physicians and the suppliers of medications for over two thousand years. The commerce driven by dis-ease is an important factor underpinning or inhibiting the recognition of disorders. Within this commercial domain, advocates of specific treatments and advocates of cocktail treatments have struggled in a dynamic that can be traced back over centuries, and this dynamic is one of the most profound cultural forces in our world today.

The Mania of Hippocrates³

Hippocrates was the first to put mania and melancholia on our cultural radar. Our story opens at Meliboea where: “a young man who had been running a temperature for a long time as a result of drinking and sexual indulgence took to his bed. His symptoms were shivering, insomnia, nausea, and lack of thirst”. He is then described as being beside himself (πάρεκρουσεν) on the 10th day. “On the 14th day his symptoms generally became more pronounced and he was beside himself and raving. On the 20th day he went mad. There was much tossing about. On the 24th day he died. This was a case of frenzy⁴ (φρενιτις)⁵”.

³ Lloyd GER (ed) (1950). Hippocratic Writings. Trans Chadwick J, Mann WN, Penguin Books Harmondsworth Middlxs.

⁴ The various translations of Hippocrates writings are historically uninformed and correspondingly inaccurate. The vignettes presented here are translated by the author and supplemented by Lloyd GER (ed) (1950). Hippocratic Writings. Trans Chadwick J, Mann WN, Penguin Books Harmondsworth Middlxs. P 138. as well as the Greek text and French translations available on http://www.bium.univ-paris5.fr/histmed/medica/hipp_va.htm From Hippocrates, Volume 1, Loeb Classical Library, p 276, Trans W R Jones.

⁵ The word phrenitis is translated as “brain fever” by Chadwick for instance when in most cases where fever was present Hippocrates makes this clear by using πυρετος. And Hippocrates would have had no conception of a brain or of an inflammation of the brain implied by brain fever.

There are a host of other such vignettes in Hippocrates some designated as frenzy and others as mania (μανιαν). But this is clearly a different kind of mania to the mania that typifies manic-depressive illness. And it is against this background that we need to interpret the case of the woman at Thasos, who psychiatrists today cite more than any other figure from antiquity. “A sensitive (δυσανιος)⁶ woman became unwell, having been sad (λυπης) after a loss, and although she did not take to her bed, she suffered from insomnia, loss of appetite, thirst, and nausea... [Early on the night of the first day,] she became frightened (φοβος), began to rave and became dysthymic (δυσθυμια⁷) [and had a slight fever. In the morning she had many spasms (σπασμοι⁸); when the spasms had passed,] she talked incoherently. [She developed a series of severe pains. On the second day, she was much the same, unable to sleep and with a more marked fever].

[On the third day, the spasms ceased but she became sleepy and obtunded, followed by a return to consciousness, when] she leapt up and could not be restrained. She began raving [and showed a high fever. That night she sweated profusely all over with warm sweat. She lost her fever and] slept well, becoming collected and lucid and reaching the crisis. [On the third day her urine was black with substances floating in it. At the time of the crisis, she had a copious menstrual flow]⁹”.

Is this an early case of manic-depressive illness? Today’s clinicians argue that manic-depressive illness and schizophrenia are more likely to occur at certain times of the year such as spring and autumn, and Hippocrates notes that mania and melancholy were more likely in spring and autumn, along with epilepsy, hemorrhages, sore throats, catarrh, hoarseness, coughs, leprosy, vitiligo, ulcerative eruptions, tumors and arthritis. Fevers, heat spots, vomiting, diarrhea, and gangrene of the genitalia predominated in summer¹⁰.

But to argue that Hippocrates describes manic-depression here involves a careful selection of the facts and a gross selection of text. Lecturers today literally omit the material in brackets above. Depending on text selection and the translation of key words, this case can be made to look like manic-depressive illness. Indeed it is even claimed that Hippocrates is describing the mixed states outlined by Kraepelin over two millennia later. But this can only happen because stripped down versions of this case circulate like a virus in manic-depressive circles, and no one goes back to place this woman in context. She had a mania that like that of the youth at Meliboea could be influenced by the airs, waters and spices in the environment. When talking about these cases, Hippocrates makes

⁶ In addition to the usual difficulties translating a word, from Galen onwards there have been uncertainties about whether this is *δυσανιος* or *δυσηνιος*, which could change meaning diametrically from sensitive to insensitive.

⁷ This is rarely if ever translated as dysthymic.

⁸ Typically translated as convulsions

⁹ *ibid.*, p 134-135; see note above.

¹⁰ *ibid.*, p 215.

constant references to risks such as the risks of drinking standing water, which at certain times of the year might lead to Quartan fever¹¹. The cases invariably involved fever and often resulted in death.

There are similarities and differences between Hippocratic and modern views on health – that do not always work in favor of modernity – but the similarities do not involve manic-depressive illness. While the guiding humoral spirit behind the Hippocratic and modern complementary healthcare systems appears similar in important respects, the Hippocratic system had a distinctive feature that picks it out from other premodern views. Unlike Yin and Yang, the dhasas, and even the serotonin of popular culture, the 4 Hippocratic humors were visible. Blood was the liquor of vitality. It made the body hot and wet. Cholera was bile or the gastric juice, and it made the body hot and dry. Phlegm was all colorless secretions, as in sweat and tears, and the thickened concentrated form that appeared in illness at the nose and mouth. It made the body cold and wet. It was found in the brain, where one of its roles was to cool the ardor of the blood. Black bile, or melancholy, was the one hidden humor. It was only seen in so far as it led to the darkening of other fluids such as blood and stools. It made the body cold and dry. The spleen was the leading candidate location for this somewhat more mysterious humor. The fact that the humors were visible and could even be quantified left the Hippocratic system open to revision and development¹².

These humors had corresponding elements, which were also visible and potentially testable. Blood was linked to fire, cholera to air, phlegm to water, and melancholy to earth. The humors were in balance with the seasons, so that for instance blood was linked to summer and phlegm to winter.

The humors were not simply blood, bile and phlegm, as we know them now, but vital forces as exemplified by blood and bile. As forces or influences, they penetrated the fabric of the body to “color” individuals and peoples. In the case of blood, this might for instance literally color an individual to make them ruddy but also lead to a sanguine or lively, energetic, and robust temperament. The choleric person was bilious in nature. The term distemper was originally used to indicate a disposition that was out of balance or a crisis that stemmed from dispositional factors rather than from acute disturbances of the more visible humors – something we might now talk of in terms of personality problems rather than acute breakdowns. Μελαγχολικός (melancholic) is in fact more often used in Hippocrates to describe a disposition than a disease.

These latter ideas about dispositions have correspondences in modern neuroscience. Neurohumors such as serotonin and norepinephrine occur in the body to a much greater extent than they occur in the brain. And even within the

¹¹ *ibid.*, p 152

¹² Lloyd GR (1979). *Magic, Reason & Experience. Studies in the Origin and Development of Greek Science.* Cambridge University Press, Cambridge.

brain there is better evidence that different configurations of norepinephrine and serotonin influence our personalities than evidence that disturbances of these humors provide a chemical basis for any nervous or mood disorder¹³.

Reading Hippocrates it is difficult to avoid the impression that these physicians were interested in more than treating disease. They appeared keen to understand why we behave the way we do. This led to descriptions such as: “Those of a bilious constitution are liable to shout and cry out during the night when the brain is suddenly heated. Those of a phlegmatic constitution do not suffer in this way. Warming of the brain also takes place when a plethora of blood finds its way to the brain and boils. It courses along the blood vessels in great quantity when a man is having a nightmare and is in a state of terror. He reacts in sleep in the same way that he would if he were awake; his face burns, his eyes are bloodshot and he is as scared as when the mind is intent upon the commission of a crime. All this ceases as soon as the man wakes and the blood is dispersed again into the blood vessels”¹⁴.

Or: “Patients with fear or depression of longstanding are subject to melancholia. In melancholic diseases a flow of humors to one part of the body is dangerous, in that either apoplexy, a fit, mania or blindness will follow. The brain may be attacked by both phlegm and bile and the resulting disorder can be distinguished thus; those whose mania results from phlegm are quiet [see section on stupor below] and neither shout nor make a disturbance; those whose mania results from bile show frenzy and will not keep still, and are always up to some mischief. Such are the causes of continued mania, but fears and frenzy may be caused by changes in the brain. Such a change occurs when it is warmed and that is the effect bile has, which when flowing through the rest of the body, courses to the brain and all the blood vessels. Fright continues until the bile runs away again into the blood vessels and into the body”.

Hippocrates was unusual in allocating the brain a role in behavior in contrast to Aristotle and others who located the drivers of behavior in the heart or elsewhere. “It is the brain too which is the seat of madness and delirium, with the fears and frights which assail us often by night but sometimes even by day; it is there where lies the cause of insomnia and sleep walking, of thoughts that will not come, forgotten duties and eccentricities. All such things result from an unhealthy condition of the brain; it may be warmer than it should be or it may be colder, or moister or drier or in any other abnormal state. Moistness is the cause of madness, for when the brain is abnormal in moisture it is necessarily agitated, and this agitation prevents sight or hearing being steady. Because of this varying visual and acoustic sensations are produced, while the tongue can only describe

¹³ Tranter R, Healy H, Cattell D, Healy D (2002). Functional variations in agents differentially selective to monoaminergic systems. *Psychological Medicine* 32, 517-524

¹⁴ *Ibid.*, p 249; See also Diethelm O (1971). *Medical Dissertations of Psychiatric Interest before 1750*. Karger; Basel., pp 16.

things as they appear and sound. So long as the brain is still, a man is in his right mind¹⁵”.

But this is to some extent a trick of translation. This was not the brain as we understand it. It took no clearer form than the encephalon – that which is within the skull. The image put forward of an excess of hot bile flooding into the brain or a deficient production of cooling phlegm causing mania made sense of some of the key clinical observations that were visible in the face and head. For Hippocrates the foreheads of maniacs and melancholics would commonly have literally felt hot with the fevers that gave rise to delirious or frenzied states.

Mania was essentially delirium. Those afflicted were maniacs rather than manics. On a probabilistic basis, it could not have been anything else. Before the antibiotics, high fevers gave rise to agitated and raving states far more commonly than any “mental” disorder did. The word frenzy, stemming from the Greek φρενος, points to how things must have been. The same frenzy is at the heart of the word schizophrenia. But far from meaning a brain, φρενος covered midriff, breast, soul, mind, heart, sense, understanding, and reason¹⁶.

The contrast with frenzy or mania was not melancholia as that term might now be used but rather stupor. Stupor happened when the phlegm in the brain became overly cool, bringing behavior to a full stop. On a probabilistic basis, the most common causes of melancholia or stupor in this sense must also have been infective or states of post-infective lethargy, although conditions now known to be Parkinsonism or hypothyroidism may also have contributed. Infections, which gave rise to delirium and later lethargy, would have led to the perception that mania might be preceded by or followed by melancholia.

The argument here that it is not possible to make links between Hippocrates use of the word mania and modern bipolar disorder is not the same as saying that Hippocrates was unable to distinguish modern diseases. Modern psychiatry is making an even bigger mistake than that. Delirium, epilepsy, impotence, leprosy, and a variety of vesical, menstrual, respiratory, digestive and neurological syndromes can be picked out with confidence in Hippocrates’ writings. Other classical authors, such as Aretaeus described glycosuria, and Galen gives very clear descriptions of cataplectic stupor or catatonia, while both Galen and Hippocrates describe hysteria.

If we considering the postpartum disorders that will be dealt with further in chapter 5 some issues become clearer. Among the 42 cases in books 1 and 111 of the “Epidemics”, 16 involve women. Of the female cases, 9 stem from the postpartum period. Postpartum problems are therefore the single biggest corpus of problems Hippocrates deals with, and there is no question that Hippocrates was medically correct to finger the postpartum period as a time of risk.

¹⁵ Ibid., p 248

¹⁶ Oxford Classical Greek Dictionary (2002). Oxford University Press. Oxford.

Consider now another of his women from Thasos, who after giving birth to a daughter had loss of appetite, despondency (αθυμος), insomnia, anger, dysphoria (δυσφορια)¹⁷ and a mental state (γνωμην) that was melancholic (μελαγχολικα). On the basis of this she meets modern criteria for an affective disorder. The problem is these terms all crop up against a background of retained lochia and in the midst of an 80-day clinical saga dominated by fevers, rigors, delirium, coma, pain and ultimately death¹⁸. Only 5% of the vignette contains material that we might now think refers to a mood disorder.

These postpartum manias, as they were called for the following 2000 years, would now be termed postpartum fevers or infections. It was not until the early 19th century that physicians began to distinguish between the insanities of the postpartum period that were accompanied by fevers and quite comparable but much less common states without fever¹⁹. Furthermore classic mental illnesses such as general paralysis of the insane have since turned out to be infective disorders without a fever, while in recent years it has become clear that ulcers, tumors and other disorders may stem from infections that do not cause fevers.

Hippocrates' postpartum cases make it clear his main focus was on what we would now recognize as infections. He and his medical successors through to the 19th century were faced with the desperate facts of contagion and wondered about air, water and other sources of transmission of disease. Against a background of terrifying and lethal epidemics, what is now called manic-depressive illness was almost an irrelevance. It was a rare disorder.

In contrast the landscape we look out on now contains much fewer apparently infective disorders but is still dominated by mushrooming epidemics of ADHD, and bipolar disorder, raising questions about how these contagions spread. Our modern supposedly scientific treatments seem about as effective in containing these new epidemics as blood-letting once was for the Greeks.

Finally another Greek text that brings mania into play with a slightly different meaning is Plato's Phaedrus²⁰. In this dialogue, Plato anticipates Shakespeare's lines from *Midsummer's Night Dream* that poets whose eyes in a fine frenzy roll from earth to heaven and back again have much in common with lovers, madmen (μανιαν), and seers whose seething brains and shaping fantasies apprehend more than cool reason ever comprehends. This use of mania has little link to mental illness. It comes closer to enthusiasm, or the use later found

¹⁷ Dysphoria here in its original sense almost certainly refers to something closer to pain than to a mood state.

¹⁸ Lloyd GER (ed) (1950). Hippocratic Writings. Trans Chadwick J, Mann WN, Penguin Books Harmondsworth Middlsex. P 128 - 129.

¹⁹ Brockington IF (1996). Motherhood and Mental Illness. Oxford University Press, Oxford. Marland H (2004). Dangerous Motherhood. Insanity and Childbirth in Victorian Britain.

²⁰ www.perseus.tufts.edu/cgi-bin/ptextlookup=Plt.+Phaedrus+244b et seq (244b-245b).

in tulip-mania that hints at the delusions of crowds. This mania, as we shall see in chapter 7, can lead to putting infants on potent psychoactive medication.

From Diagnoses to Treatments

In distinguishing between delirium or frenzy involving fever and other manias that might not, Soranus of Ephesus brought closer the possibility that a Greek or Roman physician might recognize manic-depressive disease. Soranus also noted connections between melancholy and mania, but not as two poles of one disorder. Mania was a state of overactivity, in which hallucinations and delusions were common. Patients with melancholia showed “mental anguish and distress, dejection, silence and animosity towards members of the household, sometimes a desire to live and at other times a longing for death, suspicion when a plot is being hatched against them, weeping without reason, meaningless muttering and again occasional joviality”²¹.

This melancholia was seen as part of the developing picture of a chronic form of insanity without fever that was commonly focused on a fixed obsession. The problem was thought to begin the pooling of black bile in the hypochondrium. This led to an awareness of bodily symptoms and complaints, which developed into melancholia, a prodrome of mania (insanity) rather than an opposing pole to mania. Cases of melancholia that got worse might topple over into mania. On a probabilistic basis, if not describing physical illnesses here, Soranus might have been describing schizophrenia or psychotic depressions that typically show fluctuating levels of agitation and delusions, both of which are much commoner than the swings between mania and depression found in manic-depression.

The theme of melancholy toppling over into mania recurs with Aretaeus of Cappadocia, who in addition was one of the first to describe the glycosuria that is a concomitant of diabetes. In addition to citing the woman from Thasos, modern biological psychiatrists regularly cite Aretaeus to claim that manic-depressive illness was recognized in antiquity just as diabetes was and to imply thereby that it is as real a disease as diabetes is²².

Aretaeus offered the standard descriptions of melancholia as a state of “low spirits stemming from a single phantasy, a state without fever, where the understanding is turned to sorrow and despondency only. Those affected with melancholy may not all be identically affected, but they are either suspicious of poisoning, or flee to the desert from misanthropy, or turn superstitious, or end up with a hatred of life”.

²¹ See Diethelm O (1971). *Medical Dissertations of Psychiatric Interest before 1750*. Karger; Basel., pp 17-19.

²² Goodwin F K, Jamison KR (1990). *Manic Depressive Illness*. Oxford University Press, New York; Angst J, Marneros A (2001). Bipolarity from ancient to modern times: conception, birth and rebirth. *Journal of Affective Disorders* 67, 3-19.

Melancholia he noted starts with patients becoming dull, strained, dejected and unreasonably torpid, without any manifest cause. They also become peevish, dispirited, sleepless, and begin to start up from a disturbed sleep. They become prey to anxieties, as the disease worsens, when their dreams become true, terrifying and clear. Whatever they have an aversion to when awake rushes in upon their vision in sleep.

In the course of their illness these patients are prone to change their mind readily, switching from being base, mean-spirited, illiberal to a short time later being simple, extravagant and munificent; this does not happen from any virtue of the soul, but rather simply from the changeableness of the disease. But if the illness becomes more urgent, they develop hatreds, avoid others, begin to lament, and complain about life, desiring to die²³. Read one way this can be taken as a description of a disposition. Alternately, suggestions like these of overactivity can fit into any developing psychosis, including psychotic depression.

This view that an insanity or mania might appear as a development of an initially melancholic state is widely found in Roman writers²⁴. The usual connection was in terms of melancholia being an earlier stage or mild form of madness with mania being the term used for the later and more severe stages. But these terms were almost completely non-specific and little meaning would be lost from the original texts if the terms underactive and overactive insanity were substituted for melancholia and mania.

The key issue for these physicians was the visible presentations of their patients. Take for example this celebrated description from Galen of Pergamon, the key figure after Hippocrates. He describes a student: "who had worn himself out by steady application to this studies, was seized by this disease and lay as if he were wood, stretched out stiff and unbending. He gave the impression that with his eyes open he was looking at us; he did not even blink, but nonetheless he did not say anything to us. He said [later] that he heard us at the time we were speaking, not always clearly, but there were things, which he recalled. He said that he saw everyone who was present so that he was able to describe some of their actions which he had observed, but he could neither speak nor move any member"²⁵.

In this description, the features of an extraordinary condition come through with great freshness across almost 2000 years. Greek, Roman, and later medieval physicians practicing in Latin, called this state catalepsy. This was the ultimate underactive insanity. A person might remain mute, immobile and stuporose for weeks or months. When vernacular languages took over in medicine, in the

²³ Cited in Jackson SW (1986). *Melancholia and Depression*. Yale University Press, New Haven. Ct. pp 39. See other wording in Aretaeus

²⁴ Diethelm O (1971). *Medical Dissertations of Psychiatric Interest before 1750*. Karger; Basel.

²⁵ Cited in Diethelm O (1971). *Medical Dissertations of Psychiatric Interest before 1750*. Karger; Basel., pp 72-72.

English-speaking world the dominant word for this condition was stupor – until Karl Kahlbaum in the 19th century coined a new term - catatonia²⁶ (chapter 3).

Catalepsy was readily reconciled with a humoral model. Where frenzy involved an excess of bile in the brain or a deficiency of phlegm, stupor was explained in terms of an excess of thickened phlegm. Giving too much opium or giving it at the wrong time was the kind of thing that physicians from antiquity thought might lead to phlegm congealing.

What Galen and Hippocrates bring home is that physicians in antiquity often describe diseases, and even mental disorders, that can be recognized today. But they did so on the basis of the visible appearances of the disorder – the swelling, heat and redness of a tumor, the smell of urine, the mute rigidity of stupor, the frenzy of delirium. These were not diseases based on what the affected subject reported about some inner mental state. Galen also described cases of hysteria but for him, and for almost two millennia afterwards, the commonest presentation of hysteria was in the very visible form of convulsions.

With Galen, however, a new dynamic comes into play. Shortly after the Hippocratic school established an empirical form of medicine, Aristotle elaborated his philosophy and in particular his system of logic dominated by the syllogism. This put a premium on correct reasoning rather than careful observation. Galen effected a synthesis between Aristotelian and Hippocratic systems, in the process, creating a corpus of work that remained almost unquestioned for 1500 years.

The Galenic systematization of the humoral framework led to treatments that were increasingly based on the prescriptions of a model rather than the presentation of the patient. The logical and theoretical aspects of Galenic medicine are now seen as inimical to the development by observation and experiment that medicine needs. Galenism is cited as a force against which Vesalius, Paracelsus and other medical pioneers of the Renaissance had to struggle. What is much less often noted is the role of the commercial opportunities that the new synthesis threw up.

The step after diagnosis is treatment. Within the humoral framework a variety of “drug” treatments were developed of which the most famous – Theriac – was later closely linked to Galen. Roman and Greek remedies were drawn from herbs some of which were recognized to contain a sole active principle (the simples) while others were thought to contain a number of active principles. Based on the patient’s predicament, the physician would take (Rx; recipe = take) a variety of active principles and mix them. The principles were aimed at stimulating certain bodily functions or opposing others. Theriac was the most celebrated of the resulting compounds. Many versions of this contained up to

²⁶ Fink M, Taylor MA (2003). *Catatonia*. Cambridge University Press, Cambridge.

100 supposedly active ingredients. For 1500 years, this was the pre-eminent treatment for nervousness – in 21st century terms, the ultimate brand²⁷.

While Theriac seems almost the exact opposite of a modern medicine, which aims to have a single potent ingredient, appearances and rhetoric can deceive. Unless the modern medicine contains a single replacement ingredient like iron, the chances are it is a compound medicine not unlike Theriac. This is particularly true for drugs that act on the brain, which act on a multiplicity of brain systems and receptors and are better thought of as cocktail compounds rather than thought of as specific magic bullets as they are commonly portrayed.

Theriac had another similarity to modern medicines in that it and related compounds were significant factors in the trade and commerce of Western states, such as Venice. The survival of Galenism may have owed a good deal to this commercial dominance. There is little reason to believe that the merchant classes of the late Roman period or the Middle Ages would have welcomed a new science of disease any more readily than the makers of H-2 blocking antihistamines in the 1980s welcomed news that ulcers, then the cash cow of therapeutics, might be completely eliminated by antibiotics.

Commerce & Science

In the Middle Ages humoral frameworks became very elaborate and a variety of what might now be called health handbooks were developed offering advice on the correct foods to eat at particular times of the year and correct time for certain activities in order to counterbalance environmental influences. One of the most famous of these was the *Tacuinum Sanitatis*²⁸. This and other handbooks of the time contained beautiful and masterly depictions of what might be termed the health economy or health landscape of the Middle Ages. Some of the best art of the early Renaissance period went into the *Tacuinum* to illustrate combinations of seasons, herbs and dispositions, with instructions for optimal health. There was clearly a flourishing industry in health and wellbeing at a time when the explicitly medical management of serious disease was relatively impotent to effect much meaningful difference in peoples' lives.

A turning point came with the scientific revolutions of the Renaissance. The Galenic system was faced with a challenge from anatomists like Vesalius and later Willis (see chapter 2), as well as from Paracelsus and the chemical doctors who followed him. Basel was the epicenter of change. Vesalius' *Anatomy* was first published there. And in 1526, Paracelsus was appointed the professor of medicine there - only to be stripped of the title two years later, having famously burned the books of Galen, and other ancient authorities and instructed his pupils

²⁷ Porter R (1997). *The Greatest Benefit to Mankind. A medical history of humanity from antiquity to the present.* Harper Collins. London.

²⁸ *The Medieval Health Handbook, Tacuinum Sanitatis*, Edited Luisa Cogliati Arano, George Braziller, New York 1976.

that “proofs derive from my own experience and my own reasoning and not from reference to authorities”²⁹.

Paracelsus railed against the Galenic system, and argued for a more empirical medicine. But his main point of attack had to do more with the remedies in use than with the theoretical framework. “What sense would it make for a physician if he discovered the origin of diseases but could not cure or alleviate them?”³⁰ Paracelsus had two problems with Galenic remedies. He advocated the use of purified remedies, such as metals, rather than compound medicines like Theriac. He introduced the notion that for each specific illness there might be a specific remedy, although his notions of specificity were along way from ours. He further objected to the fact that physicians had handed over the compounding of remedies to apothecaries. In this way they had lost a grasp of what their remedies contained and what treatment effects they would accordingly produce³¹. In modern terms he appears to have been asking for a greater awareness by physicians of the functional changes they wished to bring about and a deployment of therapies aimed at producing such changes rather than the scattergun hit-them-with-everything approach embodied in Theriac.

The legacy of Galen was not readily overthrown. New drugs like quinine and mercury, which flew in the face of humoral predictions, were accommodated within establishment thinking. Through the 17th century medical treatises, except for a few exceptional cases such as Willis in Oxford, continue to refer primarily to authorities such as Galen rather than to actual cases physicians may have been seeing.

What we get with Paracelsus and his successors, the chemical doctors, though is a new form of attack on medicine. From the 16th century onwards, there is a growing use of new treatments such as metals and other purified chemicals that were not based on and could not readily be explained in terms of humoral frameworks. As they were slowly adopted, medicine slowly became once more responsive to observations and data³². Medicine did so because ultimately it followed the money. In boxing parlance, this was the equivalent of hitting the body to get the head to fall. Change the practice and the thinking will follow. It has been ever thus although medical history has almost exclusively focused on the scientific head and rarely on its commercial body³³.

²⁹ Paracelsus (1979). Selected Writings. Edited Jolande Jacobi, Princeton University Press, Princeton p liii.

³⁰ Paracelsus (1979). Selected Writings. Edited Jolande Jacobi, Princeton University Press, Princeton p 84.

³¹ Pagel W 1980; Ball P (2006). The Devil's Doctor. Paracelsus and the World of Renaissance Magic and Science. Wm Heinemann London.

³² Maehle A-H (1999). Drugs on Trial: Experimental Pharmacology and Therapeutic Innovation in the Eighteenth Century. Editions Rodopi, Amsterdam.

³³ Porter R, Porter D (1989). The rise of the English drugs industry: the role of Thomas Corbyn. Medical History 33, 277-295.

The clinical theses of the 16th and 17th centuries dealing with psychiatric issues continued to stress health themes from Hippocrates and Galen onwards - physical factors such as food, air and water. This cannot be seen as a biological medicine or orientation, in that biology as we know it had not been borne at the time. But slowly from the mid-1700s onwards two developments begin to shape thinking. One is an awareness of the course of disorders. This became a key issue in the evolution of modern psychiatry after the opening of the asylums in the early 1800s where the course of a patient's illness could be systematically observed over time for the first time (chapter 2). Second behaviors such as nostalgia, alcoholism, rape, insane love, homosexuality, and homicide, which require an exploration of the inner life of the subject, began to come within medical purview (chapter 2).

There was also a slow shift to a discussion of actual cases. Dissertations began to describe new cases of melancholia, epilepsy, catalepsy, somnambulism and other behavioral disorders. Some of the ideas that these cases prompted can sound remarkably modern. For instance, William Thoner from Basel described the onset of melancholy in 1590 as involving wakefulness, disturbed sleep, sluggishness, fatigue. He emphasized that there may be no obvious triggers – it can just happen in other words³⁴. This sounds very like descriptions of endogenous depression from the mid-20th century.

Heningus Unverzagt, whose dissertation was lodged in Helmstadt in 1614, talks about primary melancholy having “as its subject the brain only. The disorder in this case would arise from actual imbalance in the brain itself, or from causes, which generate melancholic matters in the brain e.g., worry, fear, frightening sights, violent imagination and wakefulness³⁵”. With a little bit of updating of its language, this could be slotted into a line-up of various formulations of the amine/serotonin theories of depression and not be picked out as anomalous, which might give readers worries about the epistemological character of some of the most cherished notions of modern psychiatry.

When they did begin to focus on their own cases, physicians found themselves pushed into almost open revolt against the dominant Galenic ideas as this quote from Christian Vater of Wittenberg in 1680 suggests: “melancholia often passes into mania and vice versa. The melancholics themselves now laugh, now are saddened, now express numberless other absurd gestures and forms of behaviour. ... It is vain to look to humors, or spirits for an explanation of this [change]³⁶”. This mockery of the older humoral models, arguably deals as much

³⁴ cited in Diethelm O (1971). *Medical Dissertations of Psychiatric Interest before 1750*. Karger; Basel., pp 32.

³⁵ Henningus Unverzagt 1614, *De Melancholia*. Helmstadt. Cited in Diethelm O (1971). *Medical Dissertations of Psychiatric Interest before 1750*. Karger; Basel. pp 33.

³⁶ C Vater cited in Diethelm O (1971). *Medical Dissertations of Psychiatric Interest before 1750*. Karger; Basel., pp 38-39

of a body blow to modern notions on the biology of mood disorders or emotional change.

The case described by Thomas Sydenham in 1681 is arguably the most compelling. This was of a woman who “shrieks irregularly, and inarticulately, and strikes her breast and has to be held down by the united efforts of the bystanders”. Sydenham went on to outline what would now be considered the dynamics behind the syndrome this woman and others suffered from. “The patients [with this condition] feel dejected. The mind sickens more than the body. An incurable despair is so thoroughly the nature of this disease, that the very slightest word of hope creates anger... They have melancholy fore-bodings. They brood over trifles, cherishing them in their anxious and unquiet bosoms. Fear, anger, jealousy, suspicion, and the worst passions of the mind arise without cause.. there is no moderation. All is caprice. They love without measure those whom they will soon hate”³⁷.

Here is a description of a syndrome characterized by such variability that Vater would have said “It is vain to look to humors, or spirits for an explanation of this [change]”. Sydenham’s description coincided with Thomas Willis’ contemporary ground-breaking research on the anatomy of the brain outlined in chapter 2. But Sydenham held little hope that brain research would help in the practice of medicine: “[Anatomy] will be no more able to direct a physician how to cure a disease than how to make a man”³⁸. It must be doubtful that Sydenham would have found his description any more readily reconciled with modern brain theories of mood disorders than he would have found it explained by the humoral models criticized by Vater, or the brain research of Willis.

Sydenham’s description of this lady and his formulation of the dynamics of cases like this pose even bigger problems than a mere threat to the amine theories of mood disorders. The condition he outlined maps beautifully onto modern criteria for borderline personality disorder. And borderline personality disorder is just the kind of disorder that enthusiasts for bipolar disorder, as will become clear, would now regard as part of the bipolar spectrum (chapter 5). Borderline disorders typically display a rapidly alternating euphoria that the modern clinician might see as mania or hypomania and melancholy that the modern clinician might see as depression.

But Sydenham called this condition hysteria. Hysteria is of course the disorder that gave rise to modern dynamic psychology just when Emil Kraepelin was formulating the concept of manic-depressive disease. Without hysteria, it is unlikely we would have had Freud and all the changes to modern and Western sensibility that he brought about. Where the Greeks had souls and bodies, as a

³⁷ Sydenham T. *The Practice of Physick*. Trans William Salmon London 1716, Cited in Diethelm O (1971). *Medical Dissertations of Psychiatric Interest before 1750*. Karger; Basel., pp 90-91.

³⁸ Cited in Zimmer, C. (2004) *Soul Made Flesh*. William Heinemann, London, pp 246.

result of the struggles of Freud and Janet with the protean manifestations of hysteria, we have minds and psyches and bodies³⁹.

Sydenham's formulation makes it clear that looking back through the historical record to the Greeks, who first described hysteria, can throw up cases with alternating phases of mania and melancholia, or overactivity and underactivity, that are clearly psychiatric cases but not so clearly manic-depressive illness. In the case of Galen's catalepsy, it is now recognized that this also swings from pole to pole. Unless every clinical state that shows variability is deemed bipolar, this would seem to fatally undermine our abilities to state with confidence what was happening in the Graeco-Roman cases extant in the literature, other than when these involved gross cases of frenzy or stupor.

With hysteria and the birth of dynamic psychiatry at the end of the 19th century, diagnosis within psychiatry changed radically. Where the Greeks had made their diagnoses based on the visible presentations of disorders, psychiatrists began to turn to words and reports of internal mental states. This culminated in America in the 1950s when an older system of diagnosis was overthrown in favor of a new dynamic psychiatry, in which even the visible signs of physical disorders, such as ulcers or the immobility of Parkinson's disease, were liable to be interpreted as manifestations of psychopathology⁴⁰.

The psychoanalytic heyday was a brief one that ended in 1980 with publication of the 3rd edition of the American Psychiatric Association's Diagnostic and Statistical Manual for Mental Disorders – DSM III. DSM III superficially appeared to reject a diagnosis based on hidden inner forces in favor of more obvious disturbances of behavior that met operational criteria. One of the new disorders for which operational criteria were provided was bipolar disorder (chapter 5).

However far from being a radical break with analysis and a return of psychiatry to mainstream medicine, or to what many described as its Kraepelinian bedrock, the new diagnoses were still based for the most part on what people said. Despite claiming to be biological, modern psychiatrists listen to words rather than look at patients. But even though words are their *métier*, these clinicians have thrown out the range of linguistic and hermeneutic tools developed during the middle years of the century to manage words, and are arguably like a musician attempting to realize a symphony with one instrument only.

Based on words, 21st century psychiatrists diagnose a range of disorders from compulsive shopping disorder, to social phobia that physicians before the 1980s had never heard of. These diagnoses are made, in the absence of diagnostic tests to point to the validity of these conditions. In the case of ADHD and bipolar

³⁹ Healy D (1993). Images of Trauma. From Hysteria to Post-traumatic Stress Disorder. Faber & Faber, London, chapters 1-3.

⁴⁰ Healy D (1993). Images of Trauma. From Hysteria to Post-traumatic Stress Disorder. Faber & Faber, London, chapters 4..

disorder in 1-2 year old children, the diagnoses are based on the words of third parties (see chapter 7). This new use of mania may mean that continuity will soon be lost between how the word is being used in the 21st century and how it was used in the 20th century. Ironically the 21st century use may end up closer to the Greek use where it connoted overactivity.

While words reign in this way, repeated surveys have shown that the most visible of psychiatric disorders, catatonia, still occurs in up to 10% of patients but that it goes unseen and undiagnosed.⁴¹ The panoply of neuropsychiatric signs on which psychiatrists like Kraepelin depended almost certainly go equally undetected. Psychiatry is in a muddle and there would seem to be scope to get things badly wrong.

Across Time

The key point to take from this selective sweep through 25 centuries of the usage of the words mania and melancholia is that modern authorities on manic-depressive disorder make a gross error when they try to effect a link between modern presentations of a disease they call bipolar disorder and ancient precedents. There is little excuse for this mistake, in that the pit into which modern commentators fall was clearly signposted a quarter of a century ago.

In 1981, in an article on the history of mania, Edward Hare put forward the view that a difference between schizophrenia and manic-depressive illness had only appeared very recently⁴². Hare's work engaged Andrew Scull who disputed the suggestion that there was anything recent about schizophrenia. Scull's magnificent response made everyone more aware of the role that the interests of the medical profession and the power of institutions might play in the history of a disease. The controversy between Hare and Scull did a great deal to put the history of psychiatry on the map.

But another important response came from German Berrios who made it clear that Hare's argument was based on a complete misreading of the word mania⁴³. Modern psychiatrists, Berrios made clear, could not assume mania has always meant what it means to them. It is not clear that many psychiatrists have heard or understood this yet.

This is not just an arcane problem in that as we shall see there were few if any patients in the Western world described as having manic-depressive disorder before the 1920s. And in America, few patients had this disease before the 1960s. Invoking Greek precedents therefore both misreads the older literature

⁴¹ Fink M, Taylor MA (2003). *Catatonia*. Cambridge University Press, Cambridge; Chalassani P, Healy D, Morriss R (2005). Presentation and frequency of catatonia in new admissions to two acute psychiatric admission units in India and Wales. *Psychological Medicine* 35, 1667-1675.

⁴² Hare, E (1981) *The Two Manias: A study of the Evolution of the Modern Concept of Mania*. *British Journal of Psychiatry* 138, 89-99

⁴³ Berrios GE (1981) *The Two Manias*. *British Journal of Psychiatry* 139, 258-259.

but also makes it difficult to understand where manic-depressive disease went for two millennia.

Few would doubt that there were individuals in antiquity affected with core features that might lead to a diagnosis of manic-depressive illness now. But, as we shall see, this condition until recently occurred in a severity that was likely to impinge on the radars of physicians at a rate of 10 new cases per million. Given that there were not many millions of people in Rome or any conurbations until quite recently, it was just not likely that manic-depressive illness would be picked up and certainly not widely recognized.

The primary concern of physicians through to Kraepelin was with epidemics. The appearance and explosive increase in lethal conditions was a problem that threatened everyone. Against these epidemics, physicians from Hippocrates, through Willis and on to Esquirol and Kraepelin, who feature in chapters 2 and 3, watched essentially powerless as these diseases took away their wives, children, friends and colleagues. Kraepelin in his Memoirs written after the First World War described as a matter of routine the deaths of several of his children through the 1880s and 1890s and close shaves with others. Epidemics removed governments and destroyed empires⁴⁴. How much of what was happening was down to biological forces or to social arrangements or individual failings? What were the vectors of transmission? These were the key questions. Medicine for these physicians was a desperate and passionate calling rather than a dry and sterile matter – but it was all too easy to see why the overwhelming nature of these hostile forces might encourage a retreat to sterile formulae.

In contrast, comparatively few of the physicians in the generations between Willis in the 1640s and Kraepelin in the 1890s will have had relatives affected by mental illness. Now however we seem subject to new epidemics of behavioral disorders that come from nowhere and seem to seize our children and relatives. Are the vectors of transmission biological, social or individual? In the face of these new threats, we seem to have no more ideas as to the mode of contagion than Hippocrates and Willis had in their days. This point of continuity with the past, this grappling of individual physicians, and others involved in health, with the fact that the new disorders may blight the lives of their families, is at least as important an aspect of disease and its impact on all of us as is the question of whether there is a continuity of particular disease entities.

In so far as having a disease depends on the expectations that go with a specific diagnosis, then the experience of modern and ancient sufferers might be entirely different. Having tuberculosis now is entirely different to the mid-19th century experience of having consumption. The one ground that can unite experiences lies in the expectations that stem from the availability or non-availability of treatments that are thought to make a difference. But this is the

⁴⁴ Kiple K (ed) (1997). *Plagues, Pox & Pestilence. Disease in History.* Weidenfeld and Nicolson, London.

ground on which commerce as well as hope and despair flourish. A ground that can leave many physicians in Africa today in the same position vis-à-vis infective epidemics as physicians from Hippocrates through to Kraepelin were, while at the same time making it seem in the West as though manic-depressive disease is one of the most pressing scourges facing humanity.

A final point of continuity with the past lies in the dialectical opposition between empirical and theoretical orientations. An empirical orientation as found in Hippocrates, Paracelsus, and later Willis and Kraepelin, commonly leads to breakthroughs, while a theoretical orientation as found in Galen and Freud attempts to integrate developments into a worldview against which people can make sense of what might be happening to them. These latter worldviews throw up commercial opportunities as such worldviews typically have implications for health and wellbeing and not just simply for the management of acute disease. But these theories also risk becoming sterile formulae and the risk for all of us faced with threatening realities is that the formulae to which we turn will be sterile. If these formulae provide commercial opportunities, there is an added risk, namely that the therapeutic establishment may become a hindrance to efforts to get to grips with new problems.

The medical establishment in Graeco-Roman times was organized in schools linked to proto clinics. Later during the Middle Ages and Enlightenment, except in some notable European centers, medicine sat largely outside of or loosely linked to universities like Oxford or Cambridge, which were institutions in the first instance devoted to the disciplines of theology and philosophy⁴⁵. Medicine during this period and indeed until mid-20th century often seemed to academicians too pragmatic, and empirical to be considered a university discipline. It was only with the commercial opportunities thrown up by research linked to biology and the pharmaceutical industry in the second half of the 20th century that the university system in America and Britain fully embraced medicine.

The flowering of academic medicine witnessed in the middle of the 20th century may turn out to have been a brief thing. When the psychopharmaceutical events that sit at the heart of this book began to unfold from 1949 onwards, Professors of Medicine or Psychiatry from Harvard, Oxford or Paris would barely have known the names of pharmaceutical companies in the field. It was unlikely that even the most senior company figures would have been invited into the inner academic sanctums. But now the biggest university names in the field are likely to be found vying for the attentions of company personnel, and the establishment arguably now sits in company boardrooms rather than universities.

Where in the 1960s physicians carried out the research on the compounds that formed potent weapons in a new medical armory, by the end of the century research had passed out of medical hands to clinical trial organizations, and key

⁴⁵ Cambridge only opened a clinical school in the 1970s.

publications were for the most part ghost-written. What would a Paracelsus make of modern physicians, whose prescribing, as we shall see in chapter 7, is constrained by guidelines rather than by their own experience? What would Hippocrates or Kraepelin have made of a world in which companies market diseases, and people with little true disability and certainly little risk of death, appear to catch fashionable diseases?