

MANIA



A Short History of Bipolar Disorder

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THE JOHNS HOPKINS UNIVERSITY PRESS
Baltimore

CONTENTS

Foreword, by Charles E. Rosenberg	xi
Preface: Stories about Mania	xv
Acknowledgments	xxiii
Chapter 1. Frenzy and Stupor	1
Chapter 2. Circling the Brain	24
Chapter 3. Circular Madness	52
Chapter 4. The Stone of Madness	89
Chapter 5. The Eclipse of Manic-Depressive Disorder	135
Chapter 6. Branded in the USA	161
Chapter 7. The Latest Mania	198
Chapter 8. The Engineers of Human Souls	219
Coda: The Once and Future Laboratory	245
Notes	253
Index	289

Frenzy and 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 disorder.¹ 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 2,000 years of history and start instead at the end of the nineteenth century when the German psychiatrist Emil Kraepelin established manic-depressive illness in its modern form.² 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 nineteenth 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 does.

But the launch of mood-stabilizing drugs for bipolar disorder in the mid-1990s means that we cannot write off these 2,000 years, because since then contemporary biological psychiatrists have invoked the past repeatedly. Their invocations suggest that mod-

ern manic-depressive illness is not set on solid ground and that 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 eighteenth and nineteenth centuries, as we shall see in chapters 5 and 6, has been similarly invoked as a prior sufferer from this illness.

If my argument that the disease was not and could not have been recognized before the nineteenth 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 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, visible signs made it reasonable to locate the problem in the body of the sick person. For us, diagnoses depend on what people say (chapter 7). As a result, we have moved into a world in which illnesses are negotiated, the consequences of which will be considered 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 it is the individual or society that is sick.

Third, whether a disease entity was recognized before the nineteenth century or not, “dis-ease” has provided a living for physicians and the suppliers of medications for more than 2,000 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, as we shall see in chapters 4 and 8.

THE MANIA OF HIPPOCRATES

Hippocrates was the first to put mania and melancholia on our cultural radar.³ 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 (πάρέκρουσεν) on the tenth 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 [φρενίτις].”⁵

A host of other such vignettes appear in Hippocrates, some diagnosed as frenzy and others as mania (μανία). But this mania is clearly different from 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, whose story (at least the unbracketed parts of the following translation) psychiatrists today cite more than any other from antiquity.

A sensitive [δυσάντιος]⁶ woman became unwell, having been sad [λύπη] 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 [φόβος], began to rave and became dysthymic [δυσθυμία]⁷ [and had a slight fever. In the morning she had many spasms (σπασμοί);⁸ 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 cause symptoms 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 summer.¹⁰

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 translated material in brackets in this passage. Depending on text selection and the translation of key words, the case of the woman of Thasos can be made to look like manic-depressive illness. Indeed, it is even claimed that Hippocrates is describing the mixed states outlined by Kraepelin more than two millennia later. But this can happen only 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 constant references to risks, such as that of drinking standing water, which at certain times of the year might lead to quartan fever.¹¹ The cases invariably involved fever and often resulted in death.

There are similarities and differences between Hippocratic and modern views on health—ones that do not always work in favor of modernity—but the similarities do not involve manic-depressive illness. Although the guiding humoral spirit behind the Hippocratic and modern complementary health care systems appears similar in important respects, the Hippocratic system had

a feature that distinguishes it from other premodern views and contemporary complementary views. Unlike Yin and Yang, the dhasas, and even the serotonin of popular culture, the four Hippocratic humors were visible. *Blood*, the liquor of vitality, made the body hot and wet. *Choler*, bile or gastric juice, 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 also 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, seen only insofar 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. But the fact that the humors were visible and could even be quantified left the Hippocratic system open to revision and development.¹²

These humors had corresponding elements, which were also visible and potentially testable. Blood was linked to fire, choler 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 literally color an individual to make him 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. Hippocrates, in fact, uses *μελαγχολικός* (melancholic) more often 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. Even within the 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 disorder.¹³

The text of Hippocrates makes it difficult to avoid the impression that these physicians were interested in more than treating disease. As the following passages suggest, they appeared keen to understand why we behave the way we do:

Those of a bilious constitution are liable to shout and cry out during the night when the brain is suddenly heated. . . . 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.

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 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.¹⁴

Hippocrates was unusual in allocating to 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. . . . 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 things as

they appear and sound. So long as the brain is still, a man is in his right mind.¹⁵

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 φρένες, points to how things must have been. The same frenzy is at the heart of the word *schizophrenia*. But far from meaning a brain, φρένες can describe midriff, breast, soul, mind, heart, sense, understanding, and reason.¹⁶

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 postinfective 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 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 Hippo-

crates' 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.

Among the forty-two cases in books I and III of Hippocrates' "Epidemics," sixteen involve women. Of the female cases, nine stem from the postpartum period, making postpartum problems the single biggest corpus of disorders discussed in his writings. Clearly, Hippocrates was medically correct to identify the postpartum period as a time of risk. Consider now another of his women from Thasos, who, after giving birth to a daughter, had loss of appetite, despondency (ἄθυμος), insomnia, anger, dysphoria (δυσφορία),¹⁷ and a mental state (γνώμην) that was melancholic (μελαγχολικά). On the basis of these symptoms, she meets modern criteria for an affective disorder. The problem is that these symptoms all occur against a background of retained lochia and in the midst of an eighty-day clinical saga dominated by fevers, rigors, delirium, coma, pain, and ultimately death.¹⁸ Only 5 percent 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 2,000 years, would now be termed postpartum fevers or infections. Not until the early nineteenth century, as we will see in chapter 5, did physicians begin to distinguish between the insanities of the postpartum period that were accompanied by fevers and the quite comparable but much less common states without fever.¹⁹ Furthermore, classic mental illnesses such as general paralysis of the insane have since been identified as 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 focus was on what we would now recognize as infections. He and his medical successors through to the nineteenth 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 dominated by mushrooming epidemics of attention deficit hyperactivity disorder (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 *Phaedrus*.²⁰ In this dialogue, Plato anticipates Shakespeare's lines from *A Midsummer Night's Dream* that poets whose eyes in a fine frenzy roll from earth to heaven and back again have much in common with lovers, madmen (μανίαν), 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 in the Netherlands' tulip mania of the seventeenth century 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 with the pooling of black bile in the hypochondrium. This led to an awareness of bodily symptoms and complaints, which de-

veloped 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 developing 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 is.²²

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 either are suspicious of poisoning, or flee to the desert from misanthropy, or turn superstitious, or end up with a hatred of life.”

Melancholia, he noted, starts with patients becoming dull, strained, dejected, and unreasonably torpid, without any manifest cause. They also become peevish, dispirited, and 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, and 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, the patients develop hatreds, avoid others, and begin to lament and complain about life, desiring to die.²³ If 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 writers.²⁴ 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 nonspecific, 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 2,000 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 stuporous for weeks or months. When vernacular languages took over in medicine, in the English-speaking world the dominant word for this condition was stupor, until Karl Kahlbaum in the nineteenth century coined a new term—catatonia (chapter 3).²⁶

Catalepsy was readily reconciled with a humoral model. Whereas 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 at the time thought might lead to phlegm congealing.

The texts of Galen and Hippocrates make clear that physicians in antiquity often described 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 his time, and for almost two millennia afterward, 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 that was dominated by the syllogism. This system 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 1,500 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 presented.

The step after diagnosis is treatment. Within the humoral framework, various “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), whereas others were thought to contain a number of active principles. Based on the patient’s predicament, the physician would take (thus Rx, the abbreviation for the Latin *recipe*, meaning “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 Theriac contained up to 100 supposedly active ingredients. For 1,500 years, this was the preeminent treatment for nervousness—in twenty-first-century terms, the ultimate brand.²⁷

Although 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 most lucrative area of therapeutics, might be completely eliminated by antibiotics.

COMMERCE AND SCIENCE

In the Middle Ages, humoral frameworks became very elaborate, and a number of health handbooks were developed offering advice on the correct foods to eat at particular times of the year and correct times for certain activities in order to counterbalance environmental influences. These handbooks contained beautiful and masterly depictions of the health economy or health landscape of the Middle Ages. One of the most famous of these books was the *Tacuinum Sanitatis*.²⁸ Some of the best art of the medieval period went into the *Tacuinum* to illustrate combinations of seasons, herbs, and dispositions, with instructions for optimal health. Thus, an industry in health and well-being was flourishing 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's *Anatomy* was first published there. In 1526 Paracelsus was appointed the professor of medicine in Basel but was stripped of the title two years later, after he famously burned the books of Galen and other ancient authorities and instructed his pupils 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 Galenic compound medicines like Theriac, and he introduced the notion that for each specific illness there might be a specific remedy (although his notions of specificity were a long way from ours). A further objection was that physicians had handed over the compounding of remedies to apothecaries and, as a result, were less familiar with what their remedies contained and their treatment effects.³¹ In modern terms, Paracelsus 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 using a potent, multipurpose compound like Theriac.

The legacy of Galen was not readily overthrown. New drugs like quinine and mercury, which seemed to contradict humoral predictions, were accommodated within establishment thinking. Through the seventeenth century, medical treatises, except for a few exceptional cases such as works by Willis in Oxford, continued 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 sixteenth century onward, 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 adopted, medicine slowly became responsive once more to observations and data.³² 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 ever been thus, although medical history has almost exclusively focused on the scientific head and rarely on the commercial body.³³

The clinical theses of the sixteenth and seventeenth centuries dealing with psychiatric issues continued to stress health themes from Hippocrates and Galen onward—physical factors such as food, air, and water. Despite this emphasis on the physical, this approach cannot be seen as a biological medicine or orientation, in that biology as we know it had not been born at the time. But slowly from the mid-1700s onward two developments begin to shape thinking. The first development, an awareness of the course of disorders, became a key issue in the evolution of modern psychiatry after the opening of the asylums in the early 1800s offered the chance to observe the course of a patient's illness systematically over time (chapters 2 and 3). Second, understanding behaviors from nostalgia through to alcoholism, rape, insane love, and homicide, all of which require some 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, and fatigue. He emphasized that there may be no obvious triggers—it can just happen.³⁴ This sounds very much like descriptions of endogenous depression from the mid-twentieth century.

Henningus Unverzagt, whose dissertation was lodged in Helmstadt in 1614, talks about primary melancholy as 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 wakefulness.”³⁵ With a bit of updating of its language, this description 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 began to focus on their own cases, physicians found themselves pushed into almost open revolt against the dominant Galenic ideas. As Christian Vater of Wittenberg in 1680 noted, “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 Vater’s mockery of the older humoral models arguably deals as much of a setback to modern notions on the biology of mood disorders or emotional change. While it is easy to relate the invariant rigidity of Parkinson’s disease to lowered dopamine in the brain, it is not clear what it is about the multiform presentations of depression, both between individuals and even within the one subject, that could conceivably correspond to a lowering of serotonin.

Perhaps the most compelling case was one described by Thomas Sydenham in 1681, that 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 from which this woman and others suffered. “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's contemporary groundbreaking research on the anatomy of the brain outlined in chapter 2. But Sydenham held little hope that brain research would help in cases like this: "[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 patient 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 (chapters 5 and 6). Borderline disorders typically display a rapidly alternating euphoria that the modern clinician might see as mania or hypomania and dysphoria 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. Whereas the Greeks had souls and bodies, we, as a result of the struggles of Freud and Janet with the protean manifestations of hysteria, have minds and psyches and bodies.³⁹

Sydenham's formulation makes it clear that looking back through the historical record to the Greeks, who first described hysteria, can produce cases with alternating phases of mania and melancholia, or overactivity and underactivity, that are clearly psychiatric but not so clearly manic-depressive. In the case of Galen's catalepsy, it is now recognized that this condition also swings from pole to pole (chapters 3 and 5). Unless every clinical state

that shows variability is deemed bipolar, this evidence would seem to fatally undermine our abilities to state with confidence what was happening in the Greco-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 nineteenth century, diagnosis within psychiatry changed radically. Whereas 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 trend culminated in the United States 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 psychopathology.⁴⁰

The psychoanalytic heyday was a brief one that ended in 1980 with publication of the third edition of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*. The *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).

Yet, 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 (see chapter 5), 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 rejected the range of linguistic and hermeneutic tools developed during the middle years of the twentieth century to manage words and are arguably like a musician attempting to realize a symphony with one instrument only.

Based on words, twenty-first-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 mania in one- and two-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 twenty-first century and how it was used in the twentieth century. Ironically, the twenty-first-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 percent 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 twenty-five 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 appeared only very recently.⁴² Hare's work engaged Andrew Scull, who disputed the suggestion that there was anything recent about schizophrenia. Scull's 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 mania.⁴³ 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. As we shall see, there were

few if any patients in the Western world described as having manic-depressive disorder before the 1920s. In the United States, few patients had this disease before the 1960s. Invoking Greek precedents therefore both misreads the older literature and 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 in chapter 3, this condition until recently occurred in a severity that was likely to impinge on the radars of physicians at an annual rate of ten new cases per million. Given that there were not many millions of people in Rome or any major population centers 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 up to the time of Kraepelin at the end of the nineteenth century was with epidemics. The appearance and explosive increase in these 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 near deaths of others. Epidemics removed governments and destroyed empires.⁴⁴ 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 seize our children and relatives. Are the vec-

tors 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.

Insofar as having a disease depends on the expectations that go with a specific diagnosis, then even though there is a continuity to the disease, the experience of modern and ancient sufferers might be entirely different. Having tuberculosis now is entirely different from the mid-nineteenth-century experience of having consumption. But one ground that can unite older and modern experiences lies in the expectations that stem from the availability or nonavailability of treatments that are thought to make a difference. This is the 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 such as AIDS as physicians from Hippocrates through to Kraepelin were, while at the same time making it seem to physicians 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 provide commercial opportunities because they typically have implications for health and well-being 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 thera-

peutic establishment may hinder our efforts to come to grips with new problems. This is the issue that will face us in chapter 8.

The medical establishment in Greco-Roman times was organized in schools linked to protoclinics. Later, during the Middle Ages and Enlightenment, except in some notable European centers, medicine was 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 philosophy.⁴⁵ Medicine during this period and indeed until the mid-twentieth century often seemed to academicians too pragmatic and empirical to be considered a university discipline. It was only with the commercial opportunities created by research linked to biology and the pharmaceutical industry in the second half of the twentieth century that the university systems in America and Britain fully embraced medicine.

The flowering of academic medicine witnessed in the middle of the twentieth century may turn out to have been a relatively brief bloom. When the psychopharmaceutical events that sit at the heart of this book began to unfold from 1949 onward, 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 in universities.

Whereas in the 1960s physicians carried out the research on the host of new 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, key publications were for the most part ghostwritten, and the rate at which new breakthroughs were being made had slowed to a trickle. In the face of this, what would a Paracelsus make of modern physicians, whose prescribing, as we shall see in chapters 7 and 8, 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 dis-

ability and certainly little risk of death, appear to catch fashionable diseases?

What, indeed, will we make of the brave new medical world that is brought into view so well by considering the fortunes of bipolar disorder? While there are continuities and discontinuities of importance to us when considering this story that stretches back to the Greeks, a specifically modern story starts in seventeenth-century England, when Thomas Willis brought the brain as we now know it into view for the first time, and Thomas Sydenham began classifying diseases. Soon afterward, lunacy came into view in a new way as the building of the asylums exposed physicians to madness in all its guises. These developments led in 1854 in Paris to descriptions of an apparently rare new illness, *folie circulaire*, which was subsumed by Karl Kahlbaum and Emil Kraepelin into bipolar disorder and manic-depressive illness. The new disorder remained rare until a controversy arose in the 1960s about whether it might respond to treatment with lithium. This dispute in which the protagonists were both concerned to rein in the pharmaceutical industry paradoxically laid the basis for an astonishing pharmaceutical company gold rush into bipolar disorders in the 1990s that has en passant transformed the way we understand ourselves and the way our physicians approach the practice of medicine, and has also raised profound questions about the intersection between science and commerce.