5 TREATMENT[1]

> The trouble that we have in psychiatry is that we treat disorders that have a very high morbidity but very low mortality. As horrible as it sounds, we would get more respect if our patients died more often of their illnesses. As it is, they sit home, quietly hallucinating or profoundly depressed, but not really calling attention to themselves or bothering anyone. If incompetent or inadequate treatment is provided, nobody really notices.
>
> —Thomas A M Kramer, Recovery vs. response (2000)

Prelude

Earlier literature is full of strategies for dealing with mood disorders, especially melancholy. One of the great English prose works of the 17th century, Robert Burton's *Anatomy of melancholy* (1621), is an encyclopaedic treatment, by a sufferer. Even before the advent of modern psychiatry, depression was handled in ways similar to present ones: supportively through verbal intervention, physically with mood-enhancing music, social activity and exercise, or with every psychoactive drug imaginable, most of them inappropriate. Among the perennial favourites have been alcohol and opiates, neither of which is properly antidepressant or antimanic. They can however often mask or mitigate symptoms by creating short-lived elation to replace depression, quasi-euphoric sedation to counter manic agitation or anxiety, or just unconsciousness to block any feeling at all. Cocaine, and more recently amphetamines and Ecstasy, are similarly used to produce or prolong euphoria; though like alcohol in quantity they often lead to serious rebound depression, and the first two at least may eventually cause brain damage and psychosis.

But while your chosen poison is working you tend not to take much thought for the morrow. Drugs that eventually produce unconsciousness are among the most popular; this is a classic short-term cure both for depression and its frequent accompaniment of almost unbearable insomnia. Some depressives suffer from hypersomnia (excessive sleep), which may be one of nature's escape hatches. Suicide is the extreme version: permanent hypersomnia.[2] However uninformed or even desperate, these interventions have a folk-therapeutic rationale—when you are high or in a dream-like state or not conscious or not alive, you are not depressed. We are more sophisticated these days, though the old strategies remain. As do the old substances, which are still often used as unprescribed adjuncts to official treatment—sometimes usefully,

---

[1]This chapter should in principle be one of the most 'objective' in the book, since it deals with available methods of treatment and what they do. But treatment of depression is not without controversy, and I have experienced a good deal and have many personal things to say. So while I have tried to keep the science as straight as possible, I have in places slipped into the ideological, self-descriptive and autobiographical. I trust these portions will be easily recogniseable and not prejudice the others.

[2]Am I suggesting that suicide should be considered a'treatment' for depression? Yes indeed, in the appropriate circumstances; but the issues are so complex that I have devoted all of chapter 8 to them.

sometimes damagingly, most usually both at the same time.

Aside from verbal intervention, which was mainly applicable to the milder forms of mood disorder, the only therapies available to psychiatrists before the middle of the 20th century were dangerous, uncontrolled, and poorly understood. The mainstays for psychotic depression or mania (as well as schizophrenia, with which they were often confused), were crude and often perilous interventions with what little was known of normal brain function: e.g. insulin-caused coma and convulsions induced either by drugs or electric current.[3] The most drastic approach, popular from the 1930s to the 1960s, was prefrontal leucotomy (called lobotomy in the US), the nearly random destruction of white-matter tracts in one or both frontal lobes. This so drastically flattened affect that neither depression nor mania were in principle possible. It led to radical personality changes, either emotionless flaccidity, or irresponsibility, childishness, disinhibition and inability to plan. (See the story of the accidental partial lobotomy of Phineas Gage in chapter 3.) Such a procedure can 'cure' depression, if what is left is only a shadow of the original person. This is no longer done; the surgeries employed now in desperate cases are much more delicate and restricted, and usually do not damage personality.[4]

This chapter surveys a sample of the standard medical treatments for depressive disorder, both unipolar and bipolar (psychotherapy, ECT and drugs). I also deal with two 'informal' ones—self-medication with alcohol and tobacco. I give a brief account of how these work, and their dangers—especially those of the informal ones. Other major themes are the difficulties arising from the delicate balance between therapeutic effects and side-effects, dependency, and the circumstances under which one might choose to be less than optimally treated.

Psychotherapy

> There is experimental evidence from measuring the hormone levels of female doves and canaries [...] that the sexual state of females is directly influenced by the vocalizations of males, the effects being integrated over a period of days. The sounds from a male canary flood through the female's ears into her brain where they have an effect that is indistinguishable from one that an experimenter can procure with a hypodermic syringe. The male's 'drug' enters the female through the portals of her ears rather than through a hypodermic, but this difference does not seem particularly telling.
>
> —Richard Dawkins, *Unweaving the rainbow* (1998)

Parts of this chapter may make it appear that I disapprove of psychotherapy and do not believe it is helpful. This is not the case. There is very good evidence that it can be exceedingly

---

[3] The latter is still done, but in a much refined form. See below.

[4] There is a harrowing history of psychosurgery and its abuses in Valenstein 1986. For a sober treatment of its current (highly restricted) practice, see Poynton & Bridges 1997. I will not deal with this very technical issue any further.

useful—for the right patients. I am in fact too ignorant to condemn it in an intellectually respectable way even if I wanted to. But I personally do not like the kind of thing it is, and have experienced just enough to reinforce my dislike and both prevent me from experiencing it any more and lead me to discuss seriously the option of doing without it as I and many others have done.[5]I do not argue against talk therapy and the therapeutic relationship as such, even though I may sound disapproving and critical at times. This is a matter of personal attitude, and the result of my ideology, temperament and social aesthetic. And it is also a laying-out of a set of views shared by many people, though it may be a minority position. But I feel I ought to make these views as explicit as possible, both for the sake of simple honesty, and because they are relatively unfamiliar, might appear eccentric and perverse, and go counter to the received wisdom. I think they should be better known, and might turn out to be helpful and even comforting to many patients. Most of my depressed friends share these attitudes in fine detail, as do some psychiatrists, so whatever else they are not just personal idiosyncrasy. This is a warning that I will not be entirely fair and 'objective', but also expressing basic philosophical positions and personal preferences. (I did this in chapters 3 and 4 as well, in espousing total materialism and the 'medical model', so the behaviour should not be unfamiliar; and I will do it again with mood stabilisers, alcohol, tobacco and dependency.)

I was once asked to address one of the regular seminar-cum-dinners of the Society of Psychiatrists of South Africa. My assigned topic was 'Language and psychiatry'. I suppose I was invited because I am a senior language-scientist with an interest in psychiatry and personal experience of psychiatric illness (as well as a reputation for mixing serious discourse with standup comedy). Anyhow, to illustrate the main point I wanted to make, I began by saying, in as deadpan a manner as possible:

> Psychiatry, of course, is a fraudulent pseudo-discipline. It's primarily a kind of sheltered employment for cranks, nutcases, charlatans and failed physicians. Most of these appear to have unhealthy preoccupations with incest, genitalia, excretion, and the generation of false memories of childhood sexual abuse. Some, especially those of the analytic or psychodynamic persuasions, are simply mythmakers and low-grade epic poets; others, such as practitioners of so-called Cognitive-Behavioural therapies, are throwbacks to the heady days of behaviourism; they put their poor victims in verbal Skinner boxes and turn out well-trained little pigeons. The whole lot are modern witch-doctors; they use quasi-magic to achieve ambiguous and untestable results.

There were some uncomfortable half-smiles at the first sentence. As the diatribe proceeded the audience began to look puzzled, then angry—why on earth did the Society invite this antipsychiatric bigot, and how much of this are we going to have to listen to? There were some subtle stirrings as people looked for the nearest exit. Just as things were getting really tense, I

---

[5]In my one encounter of any length with (very competent) psychotherapy, and a therapist I liked enormously as a person, I found the experience overall sufficiently unpleasant that, with the presenting problem unsolved, I finally quit with relief. I will never repeat it. The reasons for this will emerge later.

smiled and said 'Seriously folks ...' I then admitted that this was not a fair picture of what I really believed—or not all of it. Indeed, since I was personally acquainted with some present who were conscientious, intelligent and dedicated doctors, I could not believe it; but most of them were not to know that. Having finished my text, I proceeded to the sermon proper. I suggested that in order to make my point as clear as possible, I would have liked all of them to be wired up at the beginning to a raft of high-tech devices, with continuous real-time measurement of heart-rate, blood-pressure, cortisol and adrenaline levels, and concurrent real-time functional MRIs, especially of their limbic systems. I said that I would not have been surprised to find raised heart-rate and blood-pressure, higher than normal stress hormone levels, and more limbic glucose uptake than one might think appropriate at the beginning of a supposedly serious academic lecture. 'Your little amygdalas', I remarked archly, 'would be lit up like Christmas trees'. In other words, my purely verbal opening would have induced a physiological state of hostile arousal, with clear empirical signs in blood chemistry and brain metabolism. There was some rueful smiling and nodding, and the previous looks of hostility and distress began to subside.

There was a serious point behind this piece of cheap theatre: the often waspish ideological divide between 'biological psychiatry' and 'talk therapy' is not as clear as it is made out to be. It may not even, despite the energy some practitioners put into maintaining it, be theoretically or clinically coherent. My arguments converged on a single point: under the nondualist interpretation of the mind/body relation, all 'nonphysical' or talk therapy can only be a kind of indirect and often slow (if peculiarly nuanced) psychopharmacology.[6] And this suggests that the most economical treatment of mood disorder should be pharmacological, since this is the area we understand best.

Curiously, many of the psychiatrists present accepted this as a kind of idealised working model. But many were deeply dissatisfied, and thought my position, while technically perhaps correct, was impoverished and one-dimensional, a heartless and arid reductionism. The patient given a purely neurochemical interpretation and treatment of his condition might begin to question what seemed previously to be important pillars of selfhood: You mean I'm only a chemical machine? Where's my Spirit, my unique Self? If my moods and thinking can be altered by drugs, where and what am '*I*'? (For some reason even people who react this way appear not to note how this applies to the use of alcohol.)

One psychiatrist told me there was a serious problem in a drugs-only approach for many patients, even if it provided dramatic relief. It is not uncommon for some who are helped (or might well be helped) by drugs to stop taking them. And they do this even when the drugs seem to be improving the condition that brought them to the doctor in the first place. The reason, he said, is

---

[6] There is one major difference: talk therapy does not generally produce physical side-effects. At least there seem to be no reports of a session with a therapist causing constipation, flatulence or impotence (I owe this point to Jaime Lass). A possible counterexample: my friend L tells me she vomits every time she has to go and see her therapist. For a study of the physical effects of psychotherapy based on brain imaging, see Linden 2006.

that as soon as the disease[7] appears to be responding to purely pharmacological treatment, it loses its 'meaning' for the patient, becomes no more 'significant' than a broken leg. Conventional folk-dualism leads many people to find their psyches more important, in some quasi-mystical way more intimately 'theirs', than their bodies. They feel empty when the symptoms go away without their having gained any knowledge or insight or narrative to fill the central and energy-consuming place they held in their psychic economy. Dramatic improvement through drugs alone apparently implies that they and their emotions are 'merely' chemical. They feel reduced, mechanised, dehumanised.

I later came across an eloquent personal account in a piece by the American writer Walter Kirn (1997). After being prescribed an antidepressant in 1991, 'before depression and its chemical basis were staple topics on the morning shows', Kirn 'went to bed that night feeling slightly ashamed'. But though the drug worked brilliantly, and faster than expected, there was a backlash:

> The change was so profound it spooked me. I'd done some reading by then on neurotransmitters, and I wasn't entirely comfortable with the notion that human laughter is, at bottom, a chemical phenomenon. After hearing from several friends how much more relaxed I looked, some whip-wielding inner Puritan took over and convinced me that I should throw away my pills.
>
> At first nothing happened. My mood stayed bright. I slept. I concluded that I had a soul after all and that my moods weren't merely molecular. Then the inevitable slippage started [...] my sense of well-being sank and sank until I felt lower and darker than ever before. I went back to a doctor—a specialist this time—and asked flat out for Prozac [...] One week later I felt fully restored and resigned myself to a humbling new self-image: neurochemical robot. I felt like one of those cutaway human heads used in TV commercials for decongestants.
>
> Once I'd lost my pharmaceutical virginity, it was impossible to get it back.

After reading this I began (reluctantly) to modify some of my previous rigid attitudes toward psychotherapy. In particular, I came to realise that this loss of pharmaceutical virginity can be a genuine problem, though I found it difficult to understand why; but some of my friends have tried to help explain it to me. Perhaps the most enlightening comment was from L, who has experience of both drugs and psychotherapy, is smart enough to know better, and actually does, but nonetheless felt rather like Kirn for a long time, as she wrote me:

> This is an important point, & obviously one that requires patience: that many people find it problematic that they exist only in their neurochemicals. Perhaps what is of concern is human agency? For me, therapy has been about recognising where/when I am an agent & where/when established chemical 'behaviours' might take considerable time to respond to my 'will' and therefore might usefully be supported by corrective chemical intervention. To be honest though, it has taken me a long time to be OK about the drugs, not to feel as if I'm relying on training wheels before the ultimate big event of going it alone. Now I realise that big

[7] It is important to remember that I am talking in this chapter (and in this book generally) only about serious, chronic illnesses—not life-adjustment problems, social or marital difficulties, phobias, general unhappiness etc. that are usually the province of psychotherapists. Any negative remarks or criticisms I may make are to be understood in this context only. And in the light of my own ideology and treatment preferences—for me.

> events come & go.

I now have more sympathy (but no more empathy) for this kind of view after thinking about it and talking to a great many people, and even undergoing some psychotherapy myself; not for depression but for a phobic disorder, with the approval of my (totally pharmacological, non-therapist) psychiatrist.[8] But in rethinking this issue I am still temperamentally and intellectually drawn to the hard materialist position, particularly as laid out in a lovely little thought experiment by V.S. Ramachandran (2003: 68). He imagines himself as a 22nd century neuroscientist, watching two people making love:

> I scan Esmeralda's brain and tell you everything that's going on when she is in love with you and is making love to you. I tell you about the activity in her septum [...] and how certain peptides are released along with the affiliation hormone prolactin, etc. You might then turn to her and say, 'You mean that's all there is to it? Your love isn't real? It's all just chemicals? To which Esmeralda should respond, 'On the contrary, all this brain activity provides hard evidence that I *do* love you, that I'm not just faking it. It should increase your confidence in the reality of my love.'

It seems that individual attitude, needs, beliefs, temperament, cognitive style, situation, relationships, education, intelligence, social preferences, desire for certain kinds of outcomes and willingness to engage in directed introspection may have a critical bearing on what therapy or combination of therapies (or no therapy) is best for a particular individual. One of the most difficult problems for the mood-disordered patient, in the face of medical advice or sometimes near-coercion, is making an informed choice.

Talk-therapy vs. medication

> Having seen people not unlike ourselves respond to medicine, we experience angst and melancholy differently—our own and others'. Perhaps what Camus' Stranger suffered—his anhedonia, his sense of anomie—was a disorder of serotonin. Kierkegaard's fear and trembling and sickness unto death are at once spiritually significant and phenomenologically unremarkable, quite ordinary spectrum traits of mammals, affects whose interpretation in metaphysical terms is wholly arbitrary.
>
> —Peter D. Kramer, *Listening to Prozac* (1994)

In the early 20th century many currents in psychiatric thinking began to coalesce under the charismatic influence of Sigmund Freud. There was already a 'classical' theory, defined, as such canons are, by specific dogmas—e.g. the ultimately sexual origin of all 'neurosis', the Oedipus

[8] I mention this to avoid the accusation that I might be saying drugs are the only useful therapy and that they are good for everything. That is patently not true. I can't imagine a dysfunctional marriage or a phobia or an eating disorder or a relationship problem cured solely by drugs (though I could certainly imagine them helping certain aspects of these conditions).

complex, etc. Eventually—and characteristically—this monolith began to shatter into sects and schools and counter-monoliths and conservative vs. revisionist orthodoxies. Psychotherapies designed to deal with depression have proliferated along with the general expansion of new psychiatric theories and practices over the post-Freudian period.[9]

The so-called 'analytic' therapies (e.g. Freudian, Jungian) are long-term and 'reconstructive'. Their aim is not to 'treat a disease' (the notion 'disease' in the ordinary medical sense is alien to this kind of theory), but to remodel the personality, or bring it into a 'state of wholeness', rather than treating a particular circumscribed disorder. The end-product is supposed to be a healthier, more functional individual, or at least one who is less dysfunctional at the end of therapy than at the beginning, and has insight into the causes of his problems. But because of expense and time constraints, and changes in theory, a plethora of shorter-term therapies has developed. One, Cognitive Behavioural Therapy (CBT) is designed to help the patient change apparently unproductive or depressogenic modes of thinking and cultivate positive attitudes. Another, Interpersonal Therapy (IPT), concentrates on current rather than past events as points of attack. There are so many schools and techniques that I have no room to name them, as well as many less formal, less 'theoretical' therapies, without particular names.

While the analytic therapies are generally the province of psychiatrists or highly trained lay analysts, the other forms may be practised by non-analytical psychiatrists, psychologists, nurses and social workers. All these modes employ different, but essentially verbal interventions—more often than not on the assumption that mental disorders are fundamentally different from physical ones, in some sense not 'medical'. The mind is somehow special, accessible and treatable only through its own direct products. The goals of therapy are language-mediated changes of attitude and/or behaviour, development of insight, maturation, achievement of 'wholeness', 'individuation'—just a sample of those expressed in the literature and practice of various schools. The ideologies of talk therapy also appear to be dominated by an implicit puritanism: 'cures' are valuable only if they require *work* on the patient's part[10]. This of course implies, as does any therapeutic decision, a theory of causality; and each therapy has its own, couched in its particular jargon.

Many psychotherapists (even psychiatrists) reject or strongly discourage the use of psychoactive medications. They may condemn the 'medicalisation' of psychiatry, disparage the 'medical model' of mental illness, or see themselves engaged in a battle against 'toxic psychiatry'.

---

[9]For a good survey of psychotherapies, ranging from the plausible to the wacky, see Sutherland 1998: chapters 14-23. Sutherland writes elegantly, is a good scholar, and is at least as opinionated as I am, though he often comes to the opposite conclusions. There have been many developments, and continue to be, since Sutherland's book. Probably the best source of up-to-date information, particularly for evidence-based discussion of non-drug therapies designed to treat stress and anxiety (and to some degree depression) is a website run by the Edinburgh physician and psychotherapist James Hawkins, http://www.goodmedicine.org..uk.

[10]This negative judgement I suppose derives from my jaundiced and perhaps somewhat ignorant view of the utility of psychological 'work', as discussed below. There is evidence that for many people this kind of self-engagement can be 'empowering'; this is outwith my experience.

This attitude is now so strong and widely spread in the media that it constitutes a severe problem to many clinicians who do not think this way. One psychiatrist wrote recently on an Internet group:[11]

> I am finding in my own clinical practice the frenzied response against medicalization is hampering confidence in most often appropriate treatment of distressed individuals. Treatment can be at times an experimental process but the successes far and above outweigh the failures. We need to guard against the all too easy media tactics and agendas that use single or small numbers of anecdotal cases of the abuses of Western medicines. As we all know much media is based on what sells and fear is a potent tool.

The 'anti-medical' ideology can unfortunately lead to crass and insensitive handling of patients who would in fact be helped by drugs, but are denied them because of some therapists' unyielding and Calvinistic attitudes or plain ignorance and lack of empathy. Here is an example—one of the psychologist Stuart Sutherland's encounters with a Freudian psychoanalyst during treatment for bipolar disorder (1998: 19):

> I put up only a feeble resistance to continuing in analysis. I asked whether it would not be better to seek some form of drug treatment, but he scoffed at this: 'All that would do is to change your mood'. To anyone who has never felt real depression or anxiety, a change of mood may sound a rather trivial thing. But for many who are mentally unwell, it can be a matter of life or death.

This attitude is often communicated to patients, with potentially destructive effects. My depressed friend D was in psychoanalysis for over two decades with no discernable improvement, until she finally quit and went onto Cipramil. She wrote to me recently about a friend of hers:

> He is cracking up and I think take the fucking drugs, tell the analyst you want them now! I am trying to tell him that to take the drugs is not to trivialise your depression and anxiety. Just fucking do it (I might as well have been talking to myself from 1974-1999). Eventually, when he said, So you think I should go onto medication, I said, you know I can't decide that for you, but let me assure you that going on antidepressants doesn't stop you being depressed. It just helps you to get up in the morning (and face being unemployed, emigrated, married with kids, and very very desperate). I just saw again the exhaustion of someone who has been fighting this thing for so long that he just doesn't have the energy to take the pain any longer. But that puritan spirit. Don't take something that will help you. That's cheating.

But some patients can resist such attitudes—and if they have to probably ought to change doctors. Consider this exchange on an Internet newsgroup devoted to depression (for ethical reasons I will not identify or date it; emphases mine):

> A. Your doc doesn't believe in meds?
>
> B. No. He wanted me to stop taking Zoloft after a few weeks. I wanted to up the dosage instead, which we did. He also thinks my history, my family and all that stuff, shows that therapy is a better treatment. *I have*

[11] Costa Vakalopoulos on psychiatry.research@yahoogroups.com, 17 May 2008.

a reason to be depressed and therefore I don't need meds, my doctor seems to think.

A. I find that a bit disturbing. I don't know what you are on. Do you have any anti-anxiety drug?

B. No, *they think the anxiety is a good sign, "that means your feelings are starting to surface"*.

The logic is extraordinary. If you have a 'reason' for depression, apparently, there is no point in relieving it. (You have a reason for food-poisoning, since those eggs were contaminated with *Salmonella*; so I won't prescribe anything to make you feel better.) One wonders what this doctor thinks his function is. The same kind of perversity is apparent in the last remark: if your 'feelings are starting to surface', that could just as easily be a source of extreme distress that the doctor as healer should be trying to mitigate. Naturally I do not know the actual story behind this exchange; but it is strikingly similar to many I have heard from friends undergoing therapy. 'Opening up' is not necessarily healthy: there is always a risk that after letting it all hang out you might not be able to put it back. I present this dialogue simply as an apparent example of bad doctoring driven by an ill-conceived view of the relation between distress and its relief. I hope it is not as typical as I think it may be. I intend it not as a general condemnation of therapists, but merely as a salutary warning of what ought to be avoided, and a prelude to what follows.

On being a good non-candidate for psychotherapy

The fragmentary self-portrait in chapter 1 suggests that the 'meaning' and origins of my depression are not particularly important (though they are of interest) to me. The disease itself however *is*, so much so that I refuse to have it completely treated. Even though my chosen mode is drugs-only,[12] the lifting of symptoms for long periods (with no new 'insight' but simply because of how the chemistry is behaving) does not empty my psychic life of meaning. That I am a chemical machine (I would never say 'merely') is self-evident and unproblematic; I find the idea exciting, elegant, aesthetically pleasing. My reductionist and parsimonious turn of mind leads me to welcome the mechanical and direct way drugs—both prescribed and recreational—work to control my moods. I would not expect anything else. If my moods are chemistry, then why should the mechanism for controlling them not also be chemistry? Since there is nothing *biologically* special about the mind (though of course there is experientially and subjectively), why not treat it like any other organ, and take medicines to make the pains in it go away? I am a devoted consumer of pills; I see no difference in principle between taking psychoactive drugs for 'mental' problems and taking antacids for heartburn. My motto is that of the Dupont Corporation: 'Better Living Through Chemistry'.

For a long time I was so convinced that this was the only rational approach to the treatment of depression that it irritated me when people chose other ways, or scolded me for not

[12] Or I thought it was. See below for a reinterpretation of part of what I was doing.

seeking 'insight' into why I was depressed, real 'understanding',what the 'significance' of my symptoms was. I was criticised for using drugs as a 'crutch' rather than aiming at a 'cure', which required therapy. The general view I was exposed to has been summed up elegantly by Peter Kramer with respect to the success of Prozac (1994: 259):

> Cure by pill is seen as dehumanizing when compared with psychotherapy [..]. The problem is not that the medicine [...] fails to move people toward an adaptive interaction with reality but, rather, that it succeeds. In doing just what psychotherapy aims to do, Prozac performs chemically what has heretofore been an intimate interpersonal function.

For me of course this is precisely what was so wonderful about antidepressants at the outset, and still is; but the situation is more subtle and complex. I will return to the role of human interaction below.

It has taken me a long time to admit the possibility that other temperaments have a right to exist, and that what helps me might distress others. I can now even acknowledge that I am not *quite* as rigidly pharmacological as I thought (though still as biological and materialist). Even that some aspects of my own depression have been mitigated, and remissions induced, at least partly through intense (if nonprofessional) human encounters. So I am not as much of a pharmacological fundamentalist as I thought; but this does not entail any form of dualism, only a more subtle materialism.

But it is apparently not all that easy for most people to be comfortable with such a reductionist and physicalist attitude. Even a gifted mathematician and philosopher like Bertrand Russell thought that materialist, evolutionary atheism had and had to have distressing consequences. The world, he said, 'which Science presents for our belief', is 'purposeless [...] void of meaning' (1918: 46ff; quoted in Burtt 1954: 23n.):

> That man is the product of causes which had no prevision of the end they were achieving; that his origin, his growth, his hopes and fears, his loves and his beliefs, are but the outcome of accidental collocations of atoms; that no fire, no heroism, no intensity of thought and feeling can preserve an individual life beyond the grave [...] all these things, if not quite beyond dispute, are yet so nearly certain that no philosophy that rejects them can hope to stand. Only within the scaffolding of these truths, only on the firm foundation of unyielding despair, can the soul's habitation henceforth be safely built [...]

On the contrary, this world-view can be refreshing and liberating. If there is nobody out there, if the universe has no guiding hand, no purpose or moral content, it cannot be accused of 'cruelty'. There is nothing there but matter/energy, organisation, luck and my own actions and interactions, whatever drives them. If the universe and life have any 'meaning', it is what I choose to give them. And I do not choose to give them any, certainly not the universe or life in general. No doubt many depressives with dualist beliefs would be far worse off, not better, if they came to adopt the views I find natural and pleasing.

Russell's philosophical position would seem to be as close to 'true' as a position on such issues can be; dualism is not to me a serious option. Genuine belief in metaphysical or 'spiritual'

entities, nonphysical minds and the like, appears primitive and superstitious, less sophisticated than a willingness to believe that the world is complex, alien, inscrutable, material and unconcerned with the creatures that happen to live in it, who are contingent products of its materiality anyhow. But this prejudice does not imply that those who are helped by religious belief or practice or dualism or anything else *I* do not accept should have it taken away from them by intellectual or therapeutic *force majeure*. Nor does it imply that all therapies based on what I like to call 'suprachemical metaphors' or placeholders for presently insoluble mysteries (like the nature of the 'self' or how neurons make mind) are *per se* undesirable, ineffective or necessarily fraudulent. While few conscientious psychiatrists would *not* use medications to stabilise a seriously ill patient, there may be things that some people want out of therapy (or life) that others do not, and there are mental styles that place less emphasis on the analytical and reductionist, on knowing rather than feeling, than mine.

It would be easy to see me as coarse and philistine, a science-blinded Yahoo. This would be wrong—as one might guess from the obsessive concern with literature and music in the first two chapters. Some people are deaf to the power of music; I seem to be that way about the metaphysical or 'spiritual'. But I do not deny the existence, much less the centrality to being human, of varieties of subjective experience that seem to the experiencer not to have any spatial 'location', or (at present) any obvious chemical or neurological grounding. These are available only *as* unique and personal experiences, immaterial and numinous. I *know* intellectually that they must be the results of purely physical processes, but I *experience* them as something utterly different. The apparent contradiction is not distressing or disequilibrating, because it clearly is only apparent. Neither I nor anyone else has a satisfactory neurochemical description of love. I haven't a clue to the neurophysiology of what goes on when I hear the great C-major chord on the word *Licht* in the first chorus of Haydn's *Creation*. Physically the hairs rise on the back of my neck, but this is surely not merely 'old mammalian piloerection' (though in one sense of course it must be). It is simply an easily detectable physical correlate of a profound and indescribable experience, like a 'conversion'—drenched in magnificence and 'meaning'.[13] A neurochemical explanation (which I am sure will be possible) would be an *extra*, not a substitute, not 'unweaving the rainbow', or sinking into what Blake called 'Newton's sleep'. Quite the contrary, it would be a profound intellectual satisfaction, a parallel delight; but it would add nothing to (nor—significantly—take anything away from) the experience itself. Anything that robbed me of my ability to have such magical experiences just as they are would be damaging me profoundly. I know this not as a matter of speculation, but because I have been through long periods where my depression has done precisely that, and other periods where the drugs I took to control it did more or less the same.

---

[13]For pioneering work in the neurobiology of such experiences, see Blood & Zatorre 2001. Damasio 2003: 310 points out that the opioid antagonist naloxone prevents the feeling of 'chills' up and down the spine that some music produces for some listeners, so the endorphin systems are almost certainly involved. Maybe I'm beginning to understand my Haydn experience. We are at least beginning to see what part of the physical substrate of the aesthetic might be.

What psychotherapy is best for

Whatever the specific theory and praxis of a psychotherapeutic approach to depression, the interaction between therapist and patient is 'mind to mind' (or person to person), across a linguistic bridge. In principle, the standard mind/brain identity arguments predict that such therapies ought to work; within this restrictive framework they make perfectly good sense. They can be seen as talking to the 'mind' side of the mind/brain in its own language, rather than to the 'brain' side in (a crude version of) *its* language, which is what drugs do. And indeed there is no doubt that mind-to-mind linguistic therapies do indeed work in particular cases. Certainly for relatively minor stress-induced depressions psychotherapy alone can be extremely helpful, even 'curative'. But not as far as I can tell for major or chronic mood disorders, though medication in conjunction with certain psychotherapies may yield better results than either alone (see Sutherland 1998: chapter 22 and the literature cited later in this chapter).[14]

Language use by psychotherapists (and what it elicits from patients) is not entirely or even largely propositional. Language is more than a conduit for information; it can affect mood as much as drugs. The language-centres in the cortex are intimately linked to the limbic structures of the temporal lobe; and subcortical (limbic and brainstem) processing precedes (prefrontal and frontal) awareness of the results of that processing. In the end the distinction between psychotherapy and psychopharmacology is not between fundamentally different types of treatment (like surgery vs. medication for a heart condition). It is rather between ultimate and proximate points of attack, and of course a matter of nuance and style. You can target the mental experiences themselves through language, or you can target the neurochemical phenomena that underlie those experiences. The embedding of language and human interaction in biology makes both approaches theoretically viable; which will work best in a given case is an empirical question.

Many different stressors, transitory or recurrent, can induce depression—events from early childhood, long-lasting early traumas, late single life-events or situations, or perhaps nothing at all but a propensity for depression. But there appears to be a final common pathway, stress-induced amine dysregulation and its effects on other aspects of neurochemistry. There are studies suggesting that some forms of psychotherapy may apparently be as effective as maintenance treatment with drugs in preventing recurrence of mild to moderate depression. How could this *not* be due to intervention at different points in the causal chain? It is simply that drugs usually work faster and probably more effectively (and crudely) than words and personal interactions because they act at synapse- or receptor-level, not at the level of entire functional systems, still less in the misty arena of human feelings and relationships. But in the end they can often do pretty much the same thing.

But we are also unique individuals, and some of us need or want verbal, personal help or

[14] This is no surprise; it is in fact predictable, ultimately the equivalent of taking two different kinds of psychoactive drugs to get a better therapeutic effect.

support while our neurochemistry is being repaired, or feel better if we are given 'instructions' for changing attitudes, or are in a psychotherapeutic relationship. I happen not to like this sort of assistance (at least from strangers). But this, like much else I say, is not meant as a universal prescription. I want rather to present and clarify an alternative way of doing things, the reflection of a particular intellectual and emotional style. It is a style, however, that might well be natural, useful and congenial to more people than usually consider it, or are allowed to by their doctors. So in most of what follows my emphasis will still be on chemistry and brain function where we know enough about them to say interesting and useful things. And my discussion of treatment will rest largely on drug-based or other physical approaches , because I feel I understand them, have experienced a good number of them, and they seem to me to come closer to the bedrock of disordered mood than other therapies. At least they act nearer to the end of the causal chain, and however poorly we understand what many of them do, we can state what we do know in crisp, non-dualist language.

Among the depressed, as in any human population, there are profound individual differences in education, intelligence, insight, even interest in or desire for further insight, imagination, analytic skill, ability to grasp concepts, degree of stigmatisation of 'mental illness', toughness, sociability, dependence on others. It is neither possible nor desirable to recommend one kind of treatment for everybody. There is no convincing evidence that any form of psychotherapy is suitable as the sole treatment for serious chronic mood disorders; but I do not disparage it as complementary to medication. I do of course think in my more utopian moods that some day, when our techniques are delicate enough and we know enough, all 'mental' disorders will be treatable entirely by pharmacological or other ordinary physical means; but this does not mean I oppose psychotherapy in general, or its use along with drug treatments for disorders whose neurochemistry we are beginning to understand. I see a considerable potential value—for the right cases. Psychotherapy can help the patient to understand and come to grips with the disease and the effects of medication; it can be an ego-support, a form of continuing education, it can provide a framework in which psychoactive medications can operate at their best, and their complex effects can be tolerated and understood.

This is a suitable point to return to the problems that so many patients (and doctors) appear to have with reductionist, purely biochemical approaches to psychiatric illness. I suspect that the main reason many people appear to want something more than drugs (whether they work or not), is that the relation with the verbal therapist is a familiar and comforting kind. It is a *social* relation, it uses tools and procedures familiar to all of us. Others are not attracted by this aspect. Indeed, I find the very idea of the psychotherapeutic relationship, with its presupposed confessional intimacy with a stranger, repellent. I do not want my doctor to understand 'me as a person'; I want him to understand my disease.[15] Only a few of my very closest friends are allowed

[15]Some personal understanding may be unavoidable, where aspects of disease and personhood are so entwined as to be inseparable; but it is usually still possible to exert some control. Ideally I treat my doctor like my mechanic. He is a technician who furnishes a service, and when he's finished I whip out my credit card.

to understand *me*, to see behind whatever masks I've constructed for the sake of my privacy. Even this apparently 'open' book hides a huge amount.

On the other hand, the problems for many others centre precisely on the lack of 'sociality' in pure drug therapy, and the highly technical knowledge required to understand it in the same way one thinks one understands human relations. This is nicely summed up by Peter Kramer (1994 :298):

> To the extent that medications are important agents of personal transformation, change becomes ever less a matter of self-understanding and ever more a matter of being understood by an expert. If what is wrong with us is explained on a physiological basis, it lies in a sphere with which we are unfamiliar and with whose manipulation we are inept. As modern men and women, we may already be uncomfortable with the extent to which our surroundings, in the form of complex equipment, are beyond our ken. Now we are faced with the likelihood that introspection alone will not explain us to ourselves.

The mind, because of its apparent accessibility and familiarity, seems somehow better understood, more a matter of everyday common knowledge, than the body. Only patients like me, who insist on at least an elementary understanding of the science behind any treatment before accepting it, do not feel the kind of gulf Kramer describes between them and their cardiologist or neurosurgeon. Most patients apparently *expect* the body and its mysteries to be matters for 'science', technical, arcane, beyond lay-people. Their very incomprehensibility and high-tech charisma lend them a kind of magic, and they tolerate mechanistic tinkering without a qualm. Such people think, however, that the mental is the opposite of the mechanistic, that our minds can be understood without special knowledge. They are transparent, familiar and present to us in a way that the electrical activity of our hearts is not; they appear to 'belong to' us simply and inalienably.

Style, content and efficacy

One major difference between psychotherapy and pharmacotherapy is the extent to which the patient has to participate; without such participation the former has no chance of working. You have to engage actively in talk therapy for it to be effective, while drugs will work regardless of what you do or think, as long as you take them. So talk therapy is labour and engagement for the patient, pharmacotherapy is either none at all, or at most remembering to take your meds and learning to live with side-effects, and with the insights and memories that sometimes come to you when your mind is cleared by drugs.

My friend L (much younger than me) chose, on her GP's advice, to embark on a programme of both medication and talk therapy. Some of her comments are relevant here, since she is temperamentally quite like me. She started therapy (of a roughly 'psychodynamic' sort), but left for six months to go abroad; on her return she decided to try again, because she 'felt very adrift & my general circumstances (work/study/home/) were shapeless'. Not, interestingly,

because of her depression.[16] I asked her what therapy had done for her in general, what she felt it was about, what it focussed on, whether the depression itself, or issues perhaps related to it. She wrote:

> For most of the time I've been in therapy [a little over four years] I've also been on antidepressant medication, and I think this is another key player if therapy is to be of any use. One of the reasons I went back on the Zoloft after a year's break is that I hadn't managed to find therapy beneficial for a few months, felt both chaotic & frozen, floundering, aggressive. [My GP] said that the material processed in therapy can actually contribute to precipitating depression, and that as long as I was down I'd probably battle to get any benefit from therapy. After about a month back on Zoloft the air cleared a little & Wednesdays with G [her therapist] resumed a more productive air.
>
> The contents of our discussions are—as far as I can see—unstructured, though there are clearly recurring narratives that pop themselves up without actually having to be on an agenda. [...] I have found two functions in therapy: one has been to help me live & cope with being depressed & anxious, the other has been to help me understand why (from my history) I might be depressed & anxious, and to explore other modes of being/responding.
>
> It has fulfilled these two functions, but I wonder now if I might not be nearing the end of just how much can be achieved. When I went into therapy I hoped I'd emerge as someone else (something like going from Eeyore to Tigger), but that seems unlikely. Ultimately, I think the benefit has been to improve the way I relate to myself, to others (both significants & incidentals), and give me a better understanding of depressive behaviours (when to try to push past it , how to sit with it & not be too afraid, how to know when it's not the precursor to an episode but rather just a shit day).
>
> The content of sessions is obviously important, but equally so is just having the solid routine & consistency of same place, same time, same person, all set up for my personal well-being. I hit & missed sessions the first 2 years, but since then it's an anomaly for me to even consider not going—isn't even related to whether I want to go or not, I just do because that's the routine.

For her at least (and many others in my experience), effective talk therapy does not focus on or treat the depression itself. Its primary benefit is support and education, its ability to deal with problems in living, adjustment, personality, self-understanding, while the depression itself is being managed by drugs. I suspect this must be true in principle: verbal therapies just cannot target neurochemical dysregulations very quickly, but can help set up an infrastructure allowing the patient to make the best out of what the drugs are doing. This is not just an eccentric amateur notion; many psychiatrists think the same way. Ronald Fieve for example (1997: 201) writes:

> They [psychotherapies] undoubtedly work for some patients in whom depression is first relieved by antidepressants. Subsequent psychotherapy may aid the patient in social readjustment to problems of living. However for most people who feel recurrently depressed, the origin [...] is physical [...] and psychotherapy is not the correct primary treatment. Often the patient does not want it. The patient is not resisting exploration of his or her unconscious, but rather seems instinctively to appreciate that it is not the problems in his or her past that are causing the depression.

[16] On reading this passage and what I'd made of her letter L commented: 'Yes this is an interesting point, & I did indeed say that. I suppose I also went back because I felt there had to be more "cure" than I'd got so far'.

Or more accurately, problems in the patient's past probably *did* cause the first dysregulations that led to the depression. But by the time the symptoms have become autonomous, the history is of little or no therapeutic relevance, and awareness of it does not help. It may even be dangerous and distressing to remember something that was buried for a good reason. In this post-Freudian era we have lost our faith in the usefulness of repression; it might be healthy to get it back

And there may be a quite good reason for this 'instinctive' appreciation that digging up and 'reliving' the past may not be particularly useful or desirable. This comment in a classic neurology textbook is instructive (Bannister 1992: 580):[17]

> However causally important infantile experiences may have been, it does not follow that they are reversible by trying to live through them again in adult life. Life cannot thus be reversed, and the adult cannot be put back into infancy to develop again differently. This is not a criticism of [...] psychotherapy in general, but it means that however much account it may take of their past, it must always deal with people as they are now, and its methods must therefore often resemble those of the orthopaedic surgeon, who aims to make life easier for his patients by correcting deformities and giving support, though he can rarely hope to restore them to the state in which they would have been if they had not suffered from congenital deformity or an acquired illness.

This sums up much that appears to be wrong or at best beside the point in the search for 'insight'.

Perhaps it is unfair to attempt a generalised argument on the basis only of my own experience, but I am not alone in these attitudes. I am not convinced that it is universally possible to accept knowledge and insight in such a way that the acceptance is healing. It certainly has not been for me, except in a few very rare and special instances. What I experience when I do obtain some insight into the causes, either distant or recent, of my own depression, is generally quite abstract. It is a depersonalised version of my own experience, accessible only as a kind of third-person narrative. Oh yes, that happened to R, and curiously I, the first-person subject, remember it in some detail. Isn't that interesting? Or even harrowing, sometimes, if I work at remembering details, or write things down—but most often not. The affect bleeds away from the remembered miseries and traumas, what ought in theory to be enlightening becomes novelistic or stagey—but not very good fiction or drama. Or if, rarely, it is convincing and concrete, it teaches me nothing, merely causes distress. It certainly does not do anything for the symptoms themselves. I may of course simply be temperamentally unable to achieve the two steps beyond this archaeological tomb-opening: I stop at exposure. There is supposed to be a kind of therapeutic Trinity: recall, acceptance, healing. I remain largely unconvinced, certainly with respect to the underlying depressive disorder itself.

At least this is the way I have viewed myself and what has happened to me. But sometimes outsiders' interpretations can make one stop and think. Being fair to opposing points of view is

---

[17] An interesting comment from L on this matter: 'This is important [...] even my therapist sometimes seems to think that resistance to 'digging" is a neon sign to dig on, that a defence is at work & one should get to the origin of it. Patients need to know that they have a right to say to the therapist "back off buster", & the therapist should back off. The reason *may* be avoidance, but that also has to be respected'.

not my favourite occupation, but I may be undervaluing or even misrepresenting the role of insight and self-exploration. My friend D, who is seriously depressed, bright and perceptive, and knows me very well, wrote the following after reading an early draft of this book:

> You see, I think you don't credit the role of reflection and insight enough [...] I believe I could show that your self-analysis is not that much different from that of someone who has been in intensive psychoanalysis. In fact, I'm not convinced that anything in the way you wrote about the way you think is much different from what any sensitive psychoanalyst would say about you [...] So, when you argue against analysis as the most effective way of coping with depression, I can't disagree (having had 20 or more years of it). But – who would you be without the thinking and feeling you have done? You just did it without the conventional analytic couch.
>
> Don't misunderstand me. I think that if I hadn't gone on medication I would be dead. I have no doubt that you would be too. I am convinced by the book. I believe you. I just think you give no credit to your mind and psyche. You don't trust your own imagination, or way of thinking about the world enough to give it a starring role in the credits along with Effexor and Dr P. So kill me.

I could say a number of things here. One might be that D has misconstrued my encounters with my depression and my self, and that the drugs did all the work; insight, reflection, thinking did nothing. The prior belief that that would be the case was one of the things that kept me from even thinking of psychotherapy. I had done enough reading in some areas to come across attitudes that annoyed me intensely, and I had no desire to encounter them in the flesh. I was particularly irritated by the bland assumption of certain therapists writing on CBT that 'negative thoughts' can simply be recognised by the therapist as 'erroneous'. This seems to me to exhibit a profound arrogance, at least equal to my own. If I feel that the world and I are garbage, and the therapist does not, what evidence could there possibly be for claiming that the more 'positive' view is necessarily correct? What if it is the thoughts of the 'normal' (obviously including therapists) that are 'erroneous', because, lacking the acute and unencumbered vision granted by the disillusion of depression, they see things through rosy spectacles? Perhaps the darkness of depression provides a special clarity that the ungifted cannot attain, because they are too standardly socialised, or lack experience?

This is not just my idiosyncratic view: Stuart Sutherland (1998: 72) suggests that 'the pessimism of the depressed is often more accurate than the optimism of the normal',[18] and characterises the effects of CBT as teaching you to lie to yourself and create a rosier image of the world and yourself than is empirically warranted (201). At least antidepressants and whisky do

[18] This claim, which is somewhat controversial among psychiatrists, posits what is called 'depressive realism'. See also Keedwell 2008. Most intelligent depressives I know naturally believe in depressive realism, as I do; we reject optimism effortlessly and naturally. Note the brilliant entry for *cynic* in Ambrose Bierce's *The Devil's dictionary* (1911 [1999]): 'A blackguard whose faulty vision sees things as they are, not as they ought to be. Hence the custom among the Scythians of plucking out a cynic's eyes to improve his vision'. We would therefore enter on a course of CBT on the wrong foot, so do not. On the other hand I have known intelligent people who have profited from CBT, and its reputation in the literature is good, though I find its basic theory problematic in some ways, and its apparent claims to direct knowledge of what is 'normal' thinking intolerable.

not try to remodel my world-view or self-image; they do not argue with me or ask me to tell them about my childhood or my feelings or set me homework assignments or engage in other intrusive pursuits. And in addition therapy of this kind would simply be too much work. In medical matters my inclination is to be passive: I would rather take pills than alter my thinking.[19] And anyhow, if a therapy were to involve any 'exercises' or 'homework' or behavioural changes I am so contrasuggestible by temperament that I would not be able to bring myself to do them.

As an example of the kind of work that can be involved in the commonest type of talk therapy, here is a description from the *Wikipedia* entry on *Cognitive behavioral therapy*:

> The particular therapeutic techniques vary within the different approaches of CBT according to the particular kind of problem issues, but commonly may include keeping a diary of significant events and associated feelings, thoughts and behaviors; questioning and testing cognitions, assumptions, evaluations and beliefs that might be unhelpful and unrealistic; gradually facing activities which may have been avoided; and trying out new ways of behaving and reacting. Relaxation, mindfulness and distraction techniques are also commonly included.

See also Scott & Beck (2008). This is precisely the kind of procedure and ideology to which I strongly abreact. This paragraph alone could define why I have not engaged in standard talk therapy.

But in a way it now seems I was engaged in something of a 'psychotherapeutic' endeavour all along, if not a formal one—and still am. The writing of this book and the research it entailed were part of it; my endless and ongoing conversations with perceptive friends were another. As M wrote to me when I was working on an earlier version of this chapter, and trying to decide how to treat talk therapies, which I really did not know much about:

> I think you must own up to having had talk therapy after all [...] it will be obvious to the reader that you are an articulate communicator and although you didn't realise it until afterwards you found talking to certain understanding friends acted in much the same way that more formal talk therapies do.

What I failed to note was the potent therapeutic effect of certain kinds of human encounter and dialogue. Depression is a lonely and isolating illness. Whether or not a patient engages in any formal therapy, one of the greatest lifesavers (for those lucky enough to have them) can be insightful and critically loving partners and friends. Whatever my feelings about 'seeing a therapist', I have been subject to great deal of such support—some of it rather against my will—and it has helped enormously, as I am still finding out, and continues to do so. For me at least this kind of encounter has been a much more useful adjunct to medication than encounters with a 'real' therapist of any kind probably would have been. I have close friends who periodically rescue me from my worst moods and attitudes, and I can sometimes do the same for

[19] This is not of course the way I behave when it comes to professional philosophical and scholarly matters, where I alter my thinking constantly, but on a rational basis—according to the principles of my trade as an academic.

them. The point is that they are friends, not strangers, many of them also depressives, and I have grown and got better through these encounters.

In summary, extrapolating from my experience with friends, there is for some people a significant place for therapy, as long as it is properly understood. My impression from talking to many depressives who have used both drugs and therapy is that the drugs treat the disease, and the therapy treats the person: i.e. the problems of living with it, or being the particular person who has it. My temperament just does not require so much of the latter, though I now find that friends give me invaluable support and insight when I need them. But this is a portrait of a perhaps peculiarly analytic and self-willed, though certainly not unique, kind of personality. I have a good number of depressed friends who have chosen this way of treating their disease, and succeeded reasonably well, and feel the same innate distaste I do for the standard therapeutic encounter. And with a few exceptions they are the most helpful to me.

I must stress though that this rather negative 'ancillary only' account of therapy does not hold for everybody; those who have been helped, even perhaps partly saved by psychotherapeutic intervention will see things very differently. They may even be the majority. Kay Jamison wrote (1995: 89):

> Pills cannot, do not, ease one back into reality; they only bring one back headlong, careening, and faster than can be endured at times. Psychotherapy is a sanctuary; it is a battleground; it is a place I have been psychotic, neurotic, elated, confused, and despairing beyond belief. But, always, it is where I have believed – or have learned to believe – that I might some day be able to contend with all of this [...] It is an odd thing, owing life to pills, one's own quirks and tenacities, and this unique, strange, and ultimately profound relationship called psychotherapy.

Well yes, for her. I have tried (even if reluctantly at times) not to sanctify my distaste for therapy and insist that going it alone is the right course as universal prescription. It is just as important not to take Jamison's kind of advocacy, well-founded as it is in her own experience, that way either. We are both writing as ourselves, and our experiences are vastly different. It is simply not the case that being under a therapist's care is necessary (or not necessary).

But whatever the efficacy of psychotherapy as treatment, some fragmentary counselling may be required for patients who are confused or helpless in the face of their illness. It can help those who do not have the cold intellectual curiosity that would allow them to use reading and talking to friends and self-analysis as exclusive sources of assistance, and those who are dysfunctional and panicky, and subject to external social pressures. Counselling does not have to be carried out by dedicated therapists or be a major part of treatment; it can also be done as needed by sensitive GPs or psychopharmacologists who take their patients seriously, who know what problems are likely to arise in treatment, and can make it clear that the present horrors will most likely eventually go away. This is especially valuable during the early stages of medication, when distressing side-effects may be superimposed on the depression for weeks or months, before any sign of response.

I would however make one prescriptive addition. Whatever the ultimate choice of therapy

may be, a seriously depressed patient must have a doctor in charge, a single court of last resort, what L calls a 'psychic bank-manager'. Somebody needs to preside over the therapeutic process, follow the time-course of the illness, be available in case of distressing side-effects, drug-failures, or changes in the disease. This bank-manager should be *medically* qualified, not a psychologist, social-worker, or anyone not licenced to prescribe and change medication. Non-medical personnel may have useful, perhaps at times crucial, supportive roles, but the primary issues in depression are specialist medical ones.

Finally, I turn briefly to the evidence for efficacy of talk therapies as opposed to medication or combination therapies. To me the nagging question has always been whether they can be shown to work in the environment of a standard clinical trial. To begin with, the idea of a 'clinical trial' of a talk therapy is problematic. Even though treatment protocols may be standardised, therapists, being individual human beings, are not. Every 20mg Prozac capsule is the same as any other, but this cannot be said for every psychotherapist or patient, or every relationship that arises in therapy. It is not possible to hate one Prozac capsule and get along well with another. In addition, trials of psychotherapies are in principle different in one important way from medication trials: as far as I know there is no strictly comparable way of giving 'placebo therapy' (though sometimes a formal therapeutic protocol like CBT is tested against 'supportive' therapy). But there have nevertheless been a great number of attempts at comparing CBT in particular with drug treatment, and the results are not uniform. In searching through the literature on this topic, I have come across so many studies with opposite conclusions that I find it extremely difficult to make up my mind.[20] There is a troubling lack of comparability in many of the various trials: neither the antidepressants nor the dosages are held constant; patient populations are often different; the targets vary (remission vs. relapse vs. only residual symptoms); and the time-courses vary as well. I frankly do not know what to make of the literature, but my hunch is that the utility of CBT and other psychotherapies is primarily supportive—at least in the short term.[21]

If I had to advise any depressed friend what to do, it would be to follow Fieve's suggestion: drugs first (with close supervision), then therapy *if wanted by the patient* or if the patient seems troubled enough by side-effects of the depression itself to warrant further intervention. That is only the advice of a long-term patient of a particular type, not a professional, and based to a great extent on personal preference. My conscience at least (I think rightly) would be satisfied with this general advice.

---

[20] For a survey see DeRubeis *et al*. 1999.

[21] For a detailed study of clinical trials that suggests my view is too pessimistic, see Scott 2001. The most recent study I have seen suggests that CBT is as efficacious as antidepressants, and is more effective at reducing risk of relapse (DeRubeis *et al*. 2008). The authors also note that the two modes probably engage 'similar neural mechanisms', though each is unique in certain ways. For the most up-to-date literature at the time of writing see http://www.goodmedicine.org.uk/stressedtozest/2009/05, which contains a good deal of material suggesting that cognitive-behavioural approaches may have a powerful contribution to make to the treatment of depression.

At this point I have nothing more to say about psychotherapy; if one is interested, it is certainly worth trying, and if one is in need of personal support and attention and a social/interactive approach that one cannot get elsewhere, and drugs are not enough, it is another possible and under the right circumstances desirable and apparently effective option. For the rest of this chapter I will be concerned only with directly physical treatment.

The biological attack

> [...] what in mee is dark
> Illumin, what is low raise and support.
>
> —John Milton, *Paradise lost* (1667)

Two kinds of non-verbal intervention in the treatment of depression have shown really solid results: mood-altering medications and direct electrical interference with brain function by induced seizures (electroconvulsive therapy or ECT).[22] I will discuss only treatments that have been subject to standard clinical testing and have shown some positive results. Successful testing does not of course guarantee that a medication is either effective or safe: major clinical trials are typically underwritten by the manufacturers of the drug being tested, and negative-outcome trials are often not published. But at least a history of testing is safer than the kind of anecdotal or 'testimonial' support used to sell 'alternative' treatments (homeopathic, herbal, etc.) I will however discuss one widely used herbal treatment that is ambiguous, but has passed at least some tests.

The main classes of mood-altering medications are antidepressants proper and mood-stabilisers (lithium, antiepileptic drugs, some antipsychotics).[23] Direct electrical interference

---

[22]There have also been experimental uses of other electrical interventions including implanted pacemaker-like devices and magnetic stimulation, but describing them in this kind of book would be premature. Though transcranial magenetic stimulation (in one precise form) has recently been given the imprimatur for the treatment of major depression by the American FDA: see pn. psychiatryonline.org/cgi/content/full/43/22/2?etoc/. Another approach has been the attempt to reset internal clocks by exposure to high-intensity light, which seems to be most effective in cases of seasonal affective disorder. All have their uses, but medication is the most widely employed and effective.

[23] For a clear and well-illustrated pedagogical introduction to the biochemistry and neurophysiology of depressive disorders and how the main medications work (aimed at beginning medical students), see Stahl 2000. There is an up-to-date, scientifically sophisticated but mildly 'alternative' treatment of the whole range of mood-elevating drugs, including street drugs and many others that are not used in psychiatry in Pearce 2008. But (contrary to my elitist expectations I must say) I have found some of the best accounts of individual drugs in their entries in *Wikipedia*, and I would advise anybody prescribed a psychoactive drug, who has some scientific background, to read the relevant one. A few are not much more than rehashes of manufacturers' inserts, but this ought to be apparent from the lack of references. For an encyclopaedic but technical treatment of just about every psychoactive drug in use, see Stahl 2009.

induces controlled seizures by passing electrical currents through the brain, what used to be and sometimes still is called 'shock treatment'. It is useful in refractory cases, but it is not a first-line treatment except under very special circumstances. Since depression is characteristically accompanied by insomnia and anxiety, and may go along with panic disorder or have psychotic episodes, antidepressants and mood-stabilisers are often supplemented with anxiolytics, antipsychotics, tranquillisers, hypnotics and other medications, as well as with ECT. Besides discussing these various treatments, I will also make some general points about psychoactive medications and their effects, and discuss in some detail the tricky issue of self-medication (alcohol and tobacco).

'Side-effects'

> Hurrah! I have been 52 hours without vomiting.
>
> —Letter from Charles Darwin to Joseph Hooker, April 1863

Any drug powerful enough to be effective against a serious disease is likely to do things other than what you want it to. Aspirin relieves pain and inflammation by inhibiting the synthesis of inflammatory messenger chemicals; but it may also have clinically irrelevant effects like compromised blood-clotting and gastric irritation. Antidepressants and other psychotropic drugs are no different. Most of them have, or can have, a significant battery of side-effects: some as it were 'incidental', like aspirin's effect on the stomach lining; others built in, because the neurotransmitters they target operate both in parts of the brain unconnected with depression, and outside as well, or have functions other than the one that treatment is targeting. The extracerebral effects (and some of the cerebral ones) may be uncomfortable and unwanted, but unavoidable. With really powerful drugs the only reason for medicating is often that the disease is even worse than the side-effects.

The side-effects of antidepressants can appear appalling. Just reading the package insert might produce some major unease. For instance the insert for Effexor says:

> The most commonly observed adverse events [...] are nervous system complaints, including headache, dizziness, dry mouth, insomnia, nervousness and somnolence; gastrointestinal complaints, including anorexia, constipation and nausea; and abnormal ejaculation/orgasm, sweating and asthenia [muscle-weakness].

Other possibilities listed are chills, abdominal and back pain, hypertension, flatulence, weight gain and/or loss, agitation, amnesia, anxiety, confusion, decreased libido, impotence, tremor, rash, pruritus [itching], and tinnitus.

Well, you might say, better to be depressed. Who wants to be anorexic, flatulent, itchy, nervous, sleepy, constipated, nauseated, sweaty, shaky, weak and impotent? Fortunately, no individual normally experiences all or even a very large number of these possible 'adverse events'; most have only a few, and these are often rather mild and many tend to decrease over time. At worst, one might be unfortunate, and find a particular drug or class of drugs intolerable.

But at best one can probably not expect to be side-effect free.

One major difficulty—for the doctor as well as the patient—is that it is impossible to tell in advance whether a given drug will work, whether it will have unbearable side-effects, and if it does, which ones. There are so many unpredictable factors: e.g. the particular dysregulation causing a patient's sickness, or whether the patient is a 'good metaboliser' or a 'poor metaboliser' of a given class of chemicals. This is genetic: some people carry mutations in genes coding for certain enzymes that make them particularly sensitive (or insensitive) to some drugs, and in those cases that we know about, the only way of accessing this information is by detailed DNA screening or elaborate biochemical testing, which is too slow and expensive to be practical, and we know too little about what we would be testing for.

There are also individual tolerance thresholds. Some people are willing or able to accept higher levels of discomfort than others. This can be related to temperament, or even to occupation: a slight sedation or cognitive blunting might not bother somebody whose life is not dependent on creativity, sustained mental alertness and quick and concentrated thinking, while it might be intolerable for an academic, scientist or artist. Stronger sedation might make a drug intolerable for someone who drives or handles machinery for a living; indeed most psychoactive drugs come with a warning about driving in the early stages.

Another problem is interaction with over-the-counter medications. It is vital for the prescribing doctor to know everything the patient might be taking for colds, hay-fever, headaches, arthritis, back-pain and indigestion. It is equally important not to take *anything*, even right off the supermarket or healthfood shop shelves, without asking the doctor. Many apparently innocent drugs may have distressing or even fatal interactions with antidepressants and other psychotropics.

One unpleasant feature of antidepressants is that the worst physical side-effects, especially the gastrointestinal ones, appear much earlier than the desired primary effects on mood. Nausea is the near-universal prelude to happiness. For this reason, it is important (but apparently not that common) for doctors to warn patients starting the relevant antidepressants about the possibility of nausea, and suggest or prescribe a safe anti-emetic. As a general rule, you can expect a waiting-period of up to six weeks for most antidepressants to achieve their full effects on mood —if they are going to—whereas some side-effects may be almost immediate..

Side-effects can lead to'non-compliance': not taking the drug as prescribed, or stopping before it has had a chance to work. The depressed patient often has a double battle at the start. In the first few weeks one is not only just as depressed as before, but often physically miserable as well. And sometimes mentally too, in new ways: many antidepressants cause agitation, anxiety and sleeplessness at the beginning; others cause sedation, many induce a general feeling of non-sedated dullness and emotional unresponsiveness. But without persevering it is impossible to find out if a particular drug is going to work or not, or be bearable. At the beginning one should be in regular contact with the prescribing doctor; many of the commonest side-effects (e.g. nausea, diarrhoea, constipation, anxiety, insomnia) can usually be easily treated. The early days of antidepressant treatment are likely not to be very pleasant, and the temptation to say the hell with it and stop can be very compelling. But it is a good idea to resist, unless the discomfort is so

distressing that it is impossible, or really alarming symptoms, like seizures, appear. There are cases where a patient's idiosyncrasies just make it impossible to continue a given drug; but there are many medications available, and treatment may require a good deal of experimentation.

It is also important to remember (though this is a long-term concern), that a drug that finally works and is tolerable may, after a period of effectiveness, suddenly start to lose its efficacy, or stop working entirely. Sometimes this merely requires an increase in dosage; at other times it may be necessary to go on to a different drug. It is not clear why this happens, or whether every case has the same causes. Occasionally this may be due to simple development of physical tolerance (as with opiates and tranquillisers): it just takes more and more drug to produce the same effect. But this is relatively uncommon. A change in the underlying chemistry of the disorder is more likely. It is also possible (but rare) for side-effects that had long vanished to return: I had to give up the best drug I'd ever taken because of this.

Antidepressants and sexual dysfunction

The most notorious and troubling side-effect of many widely used antidepressants is sexual dysfunction. This may include loss or reduction of libido (the machinery works but there is not much desire to use it), erectile dysfunction,'penile anaesthesia',[24] vaginal dryness, and inability to achieve, or extreme slowness and difficulty in achieving, orgasm. (Certain antidepressants have actually been used to treat premature ejaculation.)

Such problems however can have other causes, and these ought to be investigated as well, to make sure the antidepressant is in fact the guilty party. Depression itself can often do some of the same things, as can untreated hypertension, high cholesterol, some cholesterol-lowering drugs (you can't win), diabetes, heavy smoking and drinking. But if they first appear or worsen considerably after starting antidepressant therapy, the drug is most likely responsible. These common side-effects can be exceedingly distressing, and are one of the major reasons for noncompliance. But sometimes patients just decide to endure them because of the condition they would be in unmedicated. A friend once said to me 'I don't really care if I never get laid again; at least I'm not depressed'. A large and saddening number of my depressed friends have simply reconciled themselves to being non-sexual beings. These problems however can often be relieved, given a willingness on the part of doctors, and either money or good health insurance, or a state system that will pay for treatment of drug-induced sexual dysfunction.

One strategy reported to have good results is adding certain antidepressants (especially Wellbutrin, which is sometimes described as 'prosexual') to the current regime, or changing from the current drug to Wellbutrin. Most doctors nowadays will prescribe drugs that enhance genital blood-supply, like sildenafil (Viagra) or the longer-acting tadalafil (Cialis).One major reason for the sexually depressing effect of so many antidepressants is nature's economy—the unfortunate

[24]For Prozac: Bezchlibnyk-Butler & Jeffries 1998: 5.

fact that the same neurotransmitter may do different things in different parts of the body. Erection is largely controlled by the parasympathetic nervous system, and for this to work the sympathetic system must be switched off during the erection/lubrication sequence, and not switched on till orgasm. Many antidepressants either block the parasympathetic system or keep the sympathetic switched on all the time, or mimic its effects.

The literature on sexual dysfunction is unfortunately rather skewed toward males; the greatest concern appears to be about sporting performance. But there have been reports of efficacy of Wellbutrin in female sexual dysfunction .For more information, often quite detailed, the Internet can be quite useful: just Google 'erectile/sexual dysfunction'. Many of the sites are pitches for particular drugs, but some are more general and contain a good deal of useful information. And above all, if you have this problem see your doctor. And do not be embarrassed: you're not the only one.

Antidepressants

In general

Most antidepressants increase the quantities of circulating amine neurotransmitters—particularly serotonin and noradrenaline, less commonly dopamine. Different antidepressants may target one more than another, and they act in a variety of ways. The various pharmacological classes have different side-effects as well as varying potencies and therapeutic profiles in different patients. These are extraordinarily personal drugs, and what works well for one may be devastating or ineffective for another with apparently 'the same' illness.

Because of this and other factors, virtually all antidepressants have roughly the same aggregate response rate: roughly 70% of patients taking any given drug will respond (anywhere from slight improvement to full remission). No particular antidepressant seems to be better (in general) than any other: it depends on the patient. Some will not respond to any single drug, but might well to a combination; a certain percentage may be 'refractory' or even (rarely) completely treatment-resistant.

Many idiosyncrasies in drug response may well be due to biochemical differences in people's depressions, or to individual metabolic quirks or chemical sensitivities. For instance, the drugs that did not work for me were relatively selective for serotonin, and had much weaker effects on other neurotransmitters. The two that did work were less specific, and in particular were noradrenaline and dopamine agonists. Some patients respond well to relatively narrow-spectrum drugs like Prozac or Zoloft, others to broader-spectrum drugs like Aurorix or Effexor or the tricyclics. Even the same patient may respond differently at different times to the same drug. At present there seems no clinically practical way to tell in advance what the best drug will be: doctors have to work empirically rather than theoretically in treating depression. With all the science we have, the clinician still has to practice something of an art.

The discussion in the following sections is somewhat technical; but the information is not

widely available in general treatments of depression, and some of the issues raised are important. The science-phobic reader (if any are still here after chapters 3 and 4) can skip the details. I apologise in advance for listing characteristic side-effects: this is not designed to put the reader off (far from it), but to give some warning of the difficulties that just might emerge in treatment. Much of the material on drug action is derived from package inserts and medical literature; a good deal else is anecdotal, reflecting my experience or my friends' with particular drugs.

The major antidepressant types

There are two basic types of antidepressants. The majority are so-called reuptake inhibitors; these primarily affect the transporter proteins that remove amines from the synapse after they have triggered their downstream receptors. Some also sensitise downstream receptors and/or interfere with the feedback mechanism by which upstream neurons recognise how much neurotransmitter they have released.[25] The second major class is the monoamine oxidase inhibitors; these disable the enzymes that degrade amines after release. In most general discussions, antidepressants are chronologically classified by 'generation'. The first generation is the standard monoamine oxidase inhibitors (MAOIs) and the early tricyclics (TCAs). The second is newer TCAs and related drugs with different structures but rather similar action, and generally lower side-effect profiles. The third generation is the Selective Serotonin Reuptake Inhibitors (SSRIs: Prozac and its relatives), one new kind of MAOI, and a number of chemically heterogenous drugs sometimes loosely called 'atypicals'. But I think a biochemical approach is more informative. Following recent practice (e.g. Stahl 2000) I will discuss the most widely used antidepressants in terms of their mechanisms, starting with the tricyclics; this should also help to make some sense of the varying therapeutic and side-effect profiles.

It might be useful to recall—crudely—the typical symptoms accompanying dysregulation of the three major amine systems (based in part on Stahl 2000):

(a) *Serotonin dysregulation*: depressed mood; anxiety and/or panic; aggressiveness; phobias; obsessions and compulsions; eating disorders, particularly bulimia.[26]

(b) *Noradrenaline dysregulation*: impaired attention and concentration; problems with working memory; slowness of information-processing; depressed mood; psychomotor retardation; fatigue.

(c) *Dopamine dysregulation*: anhedonia; impaired motivation; loss of libido, sexual

[25]A third, less typical group acts as receptor blockers; I will discuss these below as well.

[26]This term (and *anorexia* below) should not be taken to designate the eating disorders so popular in the press. These properly come with the second element *nervosa*. Bulimia (literally 'ox-hunger') is simply abnormal appetite; anorexia is lack of appetite.

dysfunction; problems with memory; psychomotor retardation.

Because of the complex ways these various neurotransmitters work in different parts of the brain as well as throughout the body, the somewhat uncontrolled augmentation produced by antidepressants can have a number of side-effects, what we might call 'overcompensations':

(a) *Serotonin overcompensation*: nausea, cramps, diarrhoea, anorexia; sweating; sexual dysfunction; agitation, restlessness, insomnia.

(b) *Noradrenaline overcompensation*: overstimulation of the sympathetic nervous system: constipation, urinary retention, dry mouth; sexual dysfunction; hypertension, increased heart-rate, tremor; hypervigilance, anxiety, agitation, insomnia, (hypo)mania.

(c) *Dopamine overcompensation*: nausea; restlessness, tics; hypersexuality, (hypo)mania, psychosis.

I now turn to the various antidepressant classes.

(I) TRICYCLIC ANTIDEPRESSANTS (TCAS)

Until quite recently, the oldest of these—e.g. imipramine (Tofranil), and amitryptaline (Tryptanol, Elavil)—have been the most widely used antidepressants; there are also newer ones, like desipramine (Norpramin) and dothiepin/dosulepine (Prothiaden). These are exceedingly 'dirty' drugs: they affect systems other than those directly involved in mood. They can be unpleasant and even dangerous at high doses, and the only thing that keeps many patients on them is the fact that they work, sometimes better than the newer drugs.

Though there are differences, in general the TCAs are to varying degrees serotonin reuptake inhibitors (SRIs) and/or noradrenaline reuptake inhibitors (NRIs). But they are also antihistamines and anticholinergics (they block certain acetylcholine receptors).Reuptake inhibition is treated in chapter 3; the others require some explanation.

Blockade of CNS histamine receptors can produce drowsiness and sedation, a 'drugged' feeling (as with many antihistamines taken for allergies), and often weight gain. The first two may be useful for depressions accompanied by sleep disorders and anxiety, especially if the drug is taken at night; but some patients remain disabled and groggy long after waking. The most unpleasant effects are probably the anticholinergic ones, which mimic the 'fight or flight' reaction. These include dry mouth, constipation, urinary retention, blurred vision, fast heartbeat and raised blood-pressure, loss of libido and sexual dysfunction.

TCAs may also cause headache, insomnia, nightmares, sweating, palpitations, tinnitus, confusion and memory problems. Some are cardiotoxic, and most can be fatal in overdose. (They are the one group of antidepressants that have been extensively used, often successfully, for

suicide.)

The relative degrees of serotonin and noradrenaline reuptake inhibition vary from drug to drug, but overall they are quite similar. TCAs tend to potentiate the effects of depressants like alcohol, hypnotics and tranquillisers.

(II) Selective Serotonin Reuptake Inhibitors (SSRIs)

These disable serotonin reuptake (even though they are called 'selective', some affect other neurotransmitters too). They are relatively 'clean', and tend to have reasonably low side-effect profiles for most patients, though reports of nausea and dizziness are common. The first SSRI was fluoxetine (Prozac); others are fluvoxamine (Luvox), citalopram (Cipramil, Celexa), paroxetine (Paxil, Aropax, Seroxat) and sertraline (Zoloft, Lustral). These are now the most widely prescribed antidepressants, usually the first choice in starting treatment. Fluoxetine and fluvoxamine are also effective for obsessive-compulsive disorder, and paroxetine for anxiety and panic disorder.

The commonest side-effects are nausea, diarrhoea, constipation and sexual dysfunction. Others include anxiety, dizziness, occasional sedation, sweating, weight-gain and tremor. They may also produce agitation and restlessness, and in bipolar patients can trigger manias or hypomanias.[27] They appear to have a very low risk of enhancing the effects of alcohol and other depressants. For most patients, one advantage of the SSRIs (except fluvoxamine) is an almost complete lack of sedation.

(III) Selective serotonin and noradrenaline reuptake inhibitors (SNRIs)

There are two currently available, venlafaxine (Effexor, Venlor), and duloxetine (Cymbalta). Effexor has a reputation for being particularly useful in depressions that have resisted other drugs, though it does have a very high side-effect profile, and many patients cannot tolerate it. Aside from dry mouth and the usual gastrointestinal problems (especially constipation) and urinary and sexual difficulty, it frequently raises blood-pressure, and produces dizziness and uncomfortable and unpredictable outbreaks of sweating (the SSRIs may do this too) and/or chills. According to the manufacturer, venlafaxine does not interact with alcohol. Duloxetine appears to be very similar, and in my experience has similar side-effects to Effexor, but perhaps milder.[28] Both drugs are highly activating and may cause agitation and insomnia.

---

[27] There is evidence that most antidepressants can trigger mania or induce rapid cycling in bipolar patients. A recent study of a group of 51 patients with refractory bipolar disorder claims that about a third of recorded manic episodes and a quarter of increases in cycling rate were likely to be antidepressant-induced (Altschuler *et al.* 1995). This is not necessarily the case; my own rapid cycling preceded any antidepressant treatment.

[28] Duloxetine has been subject in the US to an FDA warning about the possibility of urinary retention (2008).

(IV) SELECTIVE NORADRENALINE AND DOPAMINE REUPTAKE INHIBITOR (NDRI)

The one drug in this category currently prescribed is buproprion (Wellbutrin), which appears to be a stronger reuptake inhibitor for dopamine than for noradrenaline.. It is highly activating, free of sexual side-effects , and does not usually potentiate the depressant effects of alcohol. The main side-effects are nausea (dopamine activates the brain's emetic centre), headache, irritability, insomnia, vivid dreams, agitation, anxiety and increased and earlier REM sleep. I have had all of these simultaneously. It can also lower the seizure threshold, so it is potentially dangerous for patients with seizure disorders.

Buproprion (under the name Zyban) is also marketed as a first-line treatment for nicotine addiction, and both the literature and my own experience suggest that it works, at least insofar as smoking is a matter of nicotine addiction: see below under 'self-medication'). It is an antagonist at the receptor that binds nicotine, and while it is not magic it certainly does help combat craving during withdrawal .It seems (to me anyhow) to be unlike any other drug I have encountered: the raising of mood it produces feels different, a kind of clarity and brightness and springiness, totally devoid of the slight inner deadness that so many other antidepressants, even activating ones like Effexor, produce. In my experience the worst side-effects are anxiety and very vivid and distressing dreams, from which one often wakes in a panic attack. It also appears for some people to lower alcohol tolerance slightly.

(V) SELECTIVE NORADRENALINE REUPTAKE INHIBITOR (NRI)

The only one on the market appears to be reboxetine (Edronax, Vestra).This drug does not appear to affect serotonin or dopamine, but is perhaps the most selective of the 'selective' antidepressants. It seems to be particularly effective for patients whose illness manifests primarily with fatigue and apathy (not anxiety or panic, which are more connected with serotonin), and general psychomotor slowing. The most frequent side-effects are dry mouth, constipation, headache, drowsiness, dizziness, excessive sweating, insomnia and sexual dysfunction including premature ejaculation as well as impotence.

(VI) SEROTONIN 2 ANTAGONIST/SEROTONIN REUPTAKE INHIBITOR (SARI)

The only commonly used drug of this type is trazodone (Desyrel, Molipaxin) . It both blocks one serotonin receptor, and disables the reuptake pump. Trazodone may be highly sedating, so much so that some doctors do not use it except as a non-addictive hypnotic. Other doctors on the other hand find it an unproblematic and effective antidepressant, and I know of patients who functioned perfectly alertly on it. Trazodone is also probably the only genuinely sexist antidepressant: one possible side-effect is priapism (sustained and painful erections which require medical rather than the customary treatment).

(VII) α-2 RECEPTOR ANTAGONISTS

These are the only widely used receptor antagonists which are not reuptake inhibitors. The α-2 receptor occurs both on noradrenaline-producing neurons in the brainstem, and on certain presynaptic serotonin neurons as well—i.e. the latter bear receptors not only for their own output but for noradrenaline. On noradrenaline neurons, noradrenaline binding beyond a certain threshold causes production to be shut off. On serotonin neurons, noradrenaline binding causes decrease in serotonin production. The logic behind using this kind of drug as an antidepressant is that if the receptor is blocked, it will not act as a 'brake' on noradrenaline or serotonin production, so the action will be equivalent to a combined NRI/SRI. The most widely marketed drug of this class is mirtazapine (Remeron).

Mirtazapine blocks certain serotonin receptors, directing the serotonin output to the one primarily responsible for anxiolytic and antidepressant effects. Blockade of other receptor types largely prevents sexual dysfunction, as well as nausea and other GI symptoms. There is however a price to pay: antagonism at one receptor may lead to weight gain. In addition, mirtazapine is somewhat antihistaminic, and may be sedating. The sedative effects may be enhanced by alcohol (generally the case with sedating antidepressants). An older drug in this class is mianserin (Tolvon, Maprotiline),. Like mirtazapine it is antihistaminic, which accounts for its sedative effect, and is most commonly prescribed for depressions accompanied by intense anxiety. I found it mildly anxiolytic but quite sedating, to the point of causing difficulty in reading anything more challenging than relatively simple thrillers.

(VIII) MONOAMINE OXIDASE INHIBITORS

These disable monoamine oxidases, the enzymes that degrade amine neurotransmitters after they have been released.

'Classical' (nonselective) MAOIs. These, phenelzine (Nardil), tranylcypramine (Parnate) and a couple of others, are at least as dirty as the TCAs, and potentially more dangerous. Because MAOs degrade amines besides the ones targeted in depression, MAOIs unfortunately interact with many other drugs, and even worse, with certain foods, and may cause liver damage. The main problem is the 'cheese reaction', a sudden and potentially fatal rise in blood pressure due to interaction with the amino acid tyramine, found in large quantities in certain foods. These drugs prevent the destruction of one of the metabolites of tyramine, which is a potent noradrenaline agonist. A sudden noradrenaline flood can precipitate a hypertensive crisis, with flushing, severe headache, cerebral haemorrhage and sometimes death following. MAOI users have to stick to a strict diet; among the forbidden items are matured cheeses, broad beans, sauerkraut, red wine, beer, soy sauce, kippers, smoked salmon, well-hung game and liver. MAOIs may also interact dangerously, as do some of the tricyclics, with many useful antihistamines and decongestants, and some anaesthetics and analgesics. Patients taking them often have to suffer their hayfever, coughs and seasickness without recourse to the most effective remedies, as well as being forbidden Rioja

and Emmenthal. I find it hard to decide which is worse.

In addition to their interaction potential, the MAOIs have their own side-effects, which may include headache, irregular heartbeat, agitation, sedation, anticholinergic effects, confusion and photosensitivity. The combination of dangerous interactivity and food restrictions makes them difficult to take, and risky except for patients who can be trusted completely to follow the complex instructions and prohibitions they require. But there appear to be certain depressions in which they work better than any other class of antidepressant.

Reversible inhibitor of MAO-A (RIMA). Only one is now in use, moclobemide (Aurorix, Manerix, Depnil). This is a selective and reversible inhibitor of monoamine oxidase A, affecting serotonin, noradrenaline and (weakly) dopamine. It is a particularly 'smart' drug: the disabling of MAO fails almost completely in the presence of tyramine, so there is virtually no danger of the cheese reaction. Main side-effects are sleep disturbances, headache, anxiety, restlessness, irritability, gastrointestinal distress, and dry mouth. There are fewer drug interactions than with classical MAOIs, but one is important. 'Severe central nervous system adverse reactions' have been seen with cold- or cough-medications containing the cough-suppressant dextromethorphan —which is most of them. It is important to check for this ingredient in over-the-counter medications. Other interactions are 'theoretically' likely, but usually not serious: e.g. with decongestants containing pseudoephedrine. Moclobemide is quite activating, and does not appear to cause sexual dysfunction. It is advertised as not interacting with alcohol.

(IX) ON THE MARGINS: ST JOHN'S WORT

I am not sure whether this really belongs here as a 'serious' treatment for depression. I include it because it is not just a do-it-yourself 'natural' remedy (though healthfood stores stock it and it is available without prescription, and it is often chosen because of its 'naturalness'). It is also frequently prescribed by doctors, especially in northern and central Europe. St John's Wort (*Hypericum perforatum*) is a little shrubby plant with golden yellow flowers, that blooms in late June all over Eurasia and America. It has been used as a medication since the Middle Ages and is now quite popular as an antidepressant and anxiolytic. It has been subject to serious clinical trials, and the results are rather ambiguous, some trials suggesting superiority to Prozac, others suggesting no advantage over placebo. But the overall result seems to be that for mild to moderate depression it is reasonably effective.

However, it can have major side-effects, rather similar to those of SSRIs (it seems among other things to be an SRI): dizziness, confusion, sedation and gastrointestinal upsets have been reported, as have sexual dysfunction and photosensitivity. There are two good reasons not to use it, though: (a) the dosages in the various preparations available over the counter are not standardised; and (b) it interacts seriously with a very large number of other medications: it reduces blood levels of antiepileptics, antiretrovirals, cancer chemotherapy drugs, oral

contraceptives, immunosuppressives, digoxin, L-Dopa and warfarin.[29] In the US, the FDA issued a general warning about its use in 2000. It must never be taken with other antidepressants, especially MAOIs.

Diversion: the 'natural' and the 'unnatural'

I detect an epidemic muddle in many peoples' attitudes toward psychoactive (and other) medications. This muddle democratically affects both the educated and the ignorant, the intelligent and the dim. It is of some importance, as aspects of it can be dangerous for patients, if perhaps good for healthfood shops and alternative practitioners. It is also philosophically bizarre, which naturally attracts my attention. The most pervasive thread in this complex of error is the 'naturalness' argument, which one hears from apparently sensible people as well as New Agers and enthusiasts for herbal remedies who think evidence-based medicine is unnecessary. It is simply incoherent, and can be defeated on its own grounds—given a few fairly uncontroversial assumptions. The central error is using 'natural' to mean 'good and healthy'.

To begin with, health is no more natural than disease. We and our diseases have evolved together; and our pathogens have been conducting a constant arms-race with us. As they get better at causing disease we get better immune responses, and as we get better immune responses ... and so on. This perpetual arms-race has been given the evocative name of the Red Queen Effect: like the Red Queen in *Alice's adventures through the looking-glass*, we have to run as fast as we can just to stay in the same place. And surely viruses and bacteria and worms, not to mention genetic, metabolic and degenerative diseases, are as much part of nature as we are. There is a common and mistaken view that things that are 'artificial' or synthesized are somehow bad for you, whereas anything natural (i.e. not man-made) is by definition healthy and benign. This is just untrue: companies who flog their products with the slogan 'no chemicals' are simply being ignorant (on the most charitable interpretation) or disingenuous. *Everything* is a chemical (serotonin as much as Prozac), and if the formula is the same a chemical synthesized in the laboratory is identical in every way to one found in nature.[30] But the simplest counterargument to the rosy view of Nature as Good can be mounted just by examining the toxicity available in our gardens: the English Cottage Garden with its laburnum, monkshood and foxgloves could be fatal if eaten.[31] So much

[29] For information on St John's Wort see www.herbmed.com. This is an excellent site, containing only legitimate refereed publications, and is not an advocacy platform. There is also useful material in summary on www.quackwatch.com/01QuackeryRelatedTopics/DSH/stjohn.htr.

[30]There is however a good point inadvertently buried in much of the fatuous discourse on the 'natural': chemicals that are entirely man-made and new, different from anything we have been exposed to in our evolutionary past, can be uniquely dangerous, since we have evolved no means to cope with them. Good examples are organophosphate insecticides and dioxins.

[31] In fact human ingenuity appears to have been unable to make anything as toxic as the 'natural' toxin produced by the bacillus that causes botulism, certain puffer-fish (*fugu*) or the venoms of some jellyfish, snakes and the Australian blue-ringed octopus.

for that little gripe: there are deeper issues involved.

If the body and mind are chemical machines (at least at the level where intervention is possible), what could be more natural than repairing broken parts of these machines with chemicals that enhance or restore their original chemistry, and go at least some way toward bringing about the original unbroken condition ('state of nature' in a Garden-of-Eden sense)? For a human to take an antidepressant is no more unnatural than for a deer to lick salt to remedy a sodium deficiency, for a rat to eat clay if it thinks it may have been poisoned, or for a chimpanzee to eat certain plants to get rid of intestinal worms (all well attested behaviours 'in nature'). We are animals that naturally make synthetic chemicals the way spiders naturally make webs or beavers make dams; it is part of our nature to be technological animals, and to enjoy the fruits of our technology. So why should we not take advantage of the artifacts that nature has made us smart enough to invent? *Not* taking drugs to relieve illness is, in this perspective, as unnatural as refusing to use our elegant apposable thumbs for fine gripping, or our extraordinary hand/eye coordination for bowling cricket balls accurately.

Following this line could of course lead to the conclusion that for instance 'not making atomic bombs and throwing them at our enemies' is also unnatural (I owe this argument to Meg Laing). I agree. We are—at least when we are being unreflective and uncontrolled— territorial, aggressive, violent, short-tempered and xenophobic, like most other primates. 'Naturalness' and what one thinks of as moral or immoral are two utterly different realms. Because something is natural does not mean it is good (or just as important, bad). To make such a claim is to commit what philosophers call the 'naturalistic fallacy': it is impossible, as it were, to derive a moral judgement from an empirical fact. All I am doing here is stressing the moral neutrality of the natural.

Mood-stabilisers

Mood-stabilisers have a levelling effect on recurrences: either manic/depressive switches, or periodic recurrences of depressive, mixed or manic episodes. All are antimanic; some are also antidepressant, others primarily anticyclic. They are chemically and biologically heterogeneous, classed together only for clinical reasons. Although some new antipsychotics are now used for stabilising purposes, the mainstays are lithium salts, and a group of drugs that used to be called 'anticonvulsants', but are now usually known as antiepileptic drugs (AEDs).

Lithium

Lithium is probably the most widely used mood-stabiliser, either alone or in combination with antidepressants and AEDs. It is still not entirely clear how it works, but it decreases excitatory neurotransmission by altering electrical activity, and either preventing or reducing neuronal firing. It also inhibits release of dopamine and noradrenaline (which partly accounts for its antimanic activity) and raises serotonin concentrations. The general effect in manic states (but unfortunately

to some degree in other states as well) is reduction of euphoria, hyperactivity, talkativeness, and libido. Many patients on lithium, even at minimum therapeutic dose, feel 'drugged' and slowed down, and cognitively and emotionally blunted. I did even on a very small dose taken not as a mood stabiliser but to augment an antidepressant, its other common use.

Lithium is often used as a monotherapy in bipolar disorder, since it has, for many patients, both antimanic and antidepressant effects. In the classical treatment model (e.g. Fieve 1997), lithium is used as the basic drug, and antidepressants added (as little as possible) when necessary, e.g. when depressive episodes break through and are not adequately controlled.

Lithium is fairly effective for acute states, but it is most commonly used as a prophylactic against further episodes. A large number of patients experience adverse effects: lethargy, fatigue, weakness, weight-gain, impairment of memory and concentration, depression, nausea, hand tremor, thirst, and urinary frequency. Most of these level out after a year or so, but some may not. Lithium has quite a few serious interactions with other drugs: in particular carbamazepine (see below), nonsteroidal anti-inflammatories (e,.g. Nurofen, Indocid), ACE inhibitors (a type of antihypertensive), and diuretics.

Lithium seems to be well-tolerated by most patients, with one major exception: it can be distressing for creative, mentally very active or high-achieving people. The following remarks from one of the earliest studies of lithium noncompliance are still relevant (Polatin & Fieve 1971, cited in Goodwin & Jamison 1990: 365). The authors note that 'the creative individual who does his best work in [...] a hypomanic period' is likely to feel that lithium

> acts as a "brake." The patients report that [it] inhibits creativity so that the individual is unable to express himself, drive is diminished, and there is no incentive. These patients also indicate that when they are depressed, the symptoms are so demoralising [...] that they welcome the "mild high" when the depression disappears and prefer to settle for a [...] life of highs and lows rather than an apathetic middle-of-the-road mood state [...]

In addition,

> never to have a high as a result of the drug seems equivalent to being deprived of an "addictive-like" pleasurable and productive state. Some of these patients are terrified of having a low again, but insist on taking their chances without lithium [...] knowing that sooner or later they will be compensated by the high, even if they do go into a low state.

This is precisely what led me to follow one psychiatrist's advice and not take lithium. Insistence on not using lithium or other mood stabilisers can be a serious point of contention between doctor and patient; I will return to this in some detail toward the end of the chapter. On the other hand, especially in patients with serious near-psychotic or psychotic manias it can, like other mood stabilisers, be a lifesaver.

Antiepileptic drugs (AEDs)

It may seem odd that drugs designed for the treatment of seizures should be used in treating mood disorder. It is even odder in light of the fact that one effective antidepressant and antimanic treatment is the *induction* of seizures (see below on ECT). But there does seem to be some relation between cyclical depressions and bipolar disorder and epilepsy—if not in the mechanism and pathology, in the patterns of recurrence (Silberstein 2000). This had been noticed as early as the 1920s by Emil Kraepelin, who suggested that there was a shared cyclical pattern in both kinds of disorders. In his model, cyclical or 'paroxysmal' disorders in general can be represented as having the following phases, endlessly repeating:

'Normal' (Quiescent disorder) ⇛ Prodrome ⇛ Severe Stage ⇛ Return to Normal

The prodrome (which does not always occur) is a 'warning' of what is to come, like an epileptic aura: e.g. hallucinations, feelings of unease, anxiety and distress, or the sense of agitation and doom that may precede a depressive episode. Similarly manic episodes may be preceded by a feeling of edginess and being 'off balance'.One major clinical point that can be drawn from this pattern is that the disease at best (unsymptomatic) is merely quiescent, not absent; or if there is a constant cyclical pattern, perhaps not even strictly speaking in remission. It is just always there, the phenomenon itself is discontinuous, and it surfaces in response to whatever exogenous or endogenous triggers restart the cycling process.

It has recently become clear that there is a kind of unholy trinity, depression, migraine and epilepsy, that have some (not yet understood) relationship. These three periodic afflictions seem to respond to an overlapping set of medications. Mood stabilising AEDs can be effective against migraine, mania, and epilepsy; TCAs and SSRIs are effective not only against depression, but also in some cases migraine. Further, a migraine sufferer runs double the normal risk of also suffering from Major Depression, three times the normal risk of mania or phobia, and four times the general risk for Anxiety Disorder. So it is not entirely surprising that drugs designed originally for seizure control should work on other recurrent disorders. The various ones on the market have different biochemical actions, but they all reduce and stabilise neurotransmission, though in quite different ways from lithium. Patients who do not respond to lithium may respond to these drugs, either alone or in combination.

The two oldest and most commonly used are carbamazepine (Tegretol) and valproate (Depakote). Both are limbic antikindling agents, which is probably why they control cycling and recurrence. Carbamazepine is chemically very like a TCA; it is antimanic, antidepressant and antipsychotic, as well as sedative and anticholinergic, and has a general depressant effect on neurotransmission. The commonest side-effects are blurred or double vision, fatigue, headache, sedation and confusion.. Valproate antagonises an enzyme which degrades the main inhibitory neurotransmitter GABA, thus raising GABA levels in the brain. It has a high side-effect profile: anorexia, hair-loss, nausea, stomach cramps, tremor and weight gain, as well as a possibility of

liver damage and interference with clotting. It may interact dangerously with other AEDs, barbiturates, anticoagulants and aspirin.

There are a number of newer drugs, which seem to be particularly effective for bipolar disorder: one of them is antimanic, another antimanic and antidepressant. Gabapentin (Neurontin) is structurally similar to GABA itself, but does not bind to receptors. It does however increase GABA concentrations, and has been shown to be effective for manic, hypomanic and mixed states. The main side-effects are transient oversedation, ataxia, visual problems, dizziness and tremor. It appears to be quite non-interactive, and may be used to augment other AEDs. Lamotrigine (Lamictin, Lamictal) antagonises glutamate (the main excitatory neurotransmitter). It appears to have a significant antidepressant effect, and is also useful in manic, hypomanic and mixed states. There is a low incidence of sexual dysfunction and weight gain; the main side effects are dizziness, tremor, somnolence, headache, nausea and rash.

Antipsychotics

These fall somewhere between antidepressants and mood stabilisers in function, though at least one in low doses seems to be a genuine antidepressant and anxiolytic. Their original and still primary use—especially for older drugs like chlorpromazine (Thorazine, Largactil) or haloperidol (Haldol)—is in treating schizophrenia and other psychotic disorders. They may also be used in psychotic phases of unipolar or bipolar depression. They are effective against mania, thought disorder, and 'flight of ideas'. Among other things they block certain dopamine receptors, which leads to a sedating and antipsychotic effect. They tend however to be rather unselective as to the part of the brain they work in: blockade of limbic dopamine receptors does reduce psychotic symptoms, but there is also antagonism in parts of the brain that control movement. This often leads to Parkinsonian side effects after long usage or high doses: tremor, stiffness, excessive salivation. Sometimes they may produce a syndrome called 'tardive dyskinesia'— an irreversible movement disorder that sets in late in treatment. They are generally unpleasant drugs to take, and in outpatient environments the rate of noncompliance is extremely high. Their place in the treatment of mood disorders is limited: clearly they are indicated only for serious psychotic states in patients where the usual mood-stabilisers have failed.

Certain newer antiposychotics however are increasingly being used in the treatment of mood disorders. Among these 'atypical' antipsychotics that are widely used are risperidone (Risperdal), clozapine (Clozaril), olanzapine (Zyprexa) and quetiapine (Seroquel). These are reputed to have fewer side-effects, and act against the so-called 'negative' symptoms of schizophrenia (poverty of speech, anhedonia, lack of motivation) as well as the 'positive' (mania, hallucination and delusion, excitement, irritability). This combination of effects has led to their use as mood stabilisers, and for the treatment of manic and hypomanic episodes in bipolar disorder. They may sometimes be substituted for antidepressants in refractory patients. I have taken Seroquel during an agitated hypomania; I found it effective but very sedating.

There is also one older antipsychotic, flupenthixol (Fluanxol), which can be effective in

low doses as an antidepressant and anxiolytic, and has little in the way of side-effects except occasional slight tremor and muscle weakness. I have used it frequently and found it to be easily tolerable and often very effective. It can be either activating or sedating, but above all does not appear to produce the slight emotional dullness and unresponsiveness that even activating antidepressants like Effexor do: it and Wellbutrin are the only two drugs I've found that do not interfere at least slightly with listening to music or reading poetry or looking at pictures.

Minor tranquillisers and hypnotics

These are not first-line treatments for depression, but for some of its accompaniments. Many depressives also suffer from agitation, severe anxiety (periodic or fairly continuous), and/or panic attacks. In addition, many antidepressants—e.g. Aurorix, the SSRIs, Effexor and Wellbutrin—may be quite activating and cause anxiety or agitation, particularly in the early stages of treatment. Anxiety symptoms, whether comorbid or treatment-induced, may be at least as disabling as depression, and must be treated along with it. Some antidepressants (e.g. classical MAOIs, paroxetine, imipramine, Effexor) are themselves anxiolytic, but this may be insufficient. Another very common accompaniment to depression itself, or to treatment with the more activating antidepressants, is insomnia. Few seriously depressed people I know can sleep without some assistance, even if their antidepressants are working. Any drug that raises the anxiety threshold, or induces relaxation and eventually sleep, can be enormously useful as part of the treatment of serious mood disorder.

For both of these problems, the drug of choice is usually one of the so-called 'minor tranquillisers' (benzodiazepines),[32] though there are two other widely used and rather different anti-anxiety drugs and some new hypnotics. The benzodiazepines, now the most widely used 'tranquillising' drugs, inhibit neurotransmission. They are all, to one degree or another, anxiolytic, muscle-relaxant, arousal-reducing and memory-inhibiting. The major side-effects are predictable: sedation, somnolence, clumsiness, loss of reactivity, and memory deficits.

They are also dependence-forming for most users, and some are extremely difficult to withdraw from. This addictive propensity often leads doctors to be somewhat wary of prescribing them, at least for long periods;[33] but many do anyhow, since they are so effective and can so

[32] The highly potent first-generation antipsychotics like Thorazine are referred to as 'major tranquillisers'.

[33] Both ordinary tranquillisers and hypnotics are typically recommended only for very short periods. This is probably alarmist; I have been taking alprazolam and the hypnotics flunitrazepam and then zopiclone and then loprazolam for over 15 years, and have not developed major tolerance, though I have certainly developed dependency. This however is not considered a serious problem, at least outside of the US and UK, which tend to be very conservative and not as enlightened as Europe and South Africa. At the 11th Congress of the European College of Neuropsychopharmacology (1999), a number of papers dealt with this. According to one presentation, a survey showed that 68% of specialists from 25 countries did not regard benzodiazepine dependence as a major problem or contraindication to long-term use. Hans-Jurgen Moeller, Professor of Psychiatry at the University of Munich, even warned that there is a risk in using low dosages for short periods. He remarked that 'there are patients who need long-term treatment. A patient suffering from GAD [Generalised

greatly enhance quality of life. The main differences among these chemically rather similar drugs are speed of onset of action, sedativeness and speed of clearance. Which one chooses depends on the desired effect: obviously a hypnotic should clear fairly quickly, to avoid morning hangover, while an anxiolytic or anti-panic agent should be longer-acting and less sedating. The general anxiolytics include such familiar longer-acting benzodiazepines as lorazepam (Ativan), diazepam (Valium), and the shorter-acting alprazolam (Xanax, Xanor, Alzam), which is effective against panic, phobias, anxiety and agitation, and appears to be mood-elevating for some patients. If it is possible to feel a deep personal affection for a drug I feel it for alprazolam: it dissolves even serious anxiety in a remarkably short time, appears to have no side-effects in low dosages, and just makes me feel indefinably better and cheerier.The benzodiazepines and the other hypnotics described below all appear to be agonists at the $GABA_A$ receptor complex; they seem to be high-powered surrogates for a natural inhibitory neurotransmitter.

The main widely used non-benzodiazepine anxiolytics are buspirone (BuSpar) and sulpiride (Eglonyl). Buspirone appears to take much longer to begin working than the benzodiazepines (up to 3 weeks), and may have similar side-effects (confusion, depression, weakness), as well as light-headedness, digestive problems, and sexual dysfunction. Unlike the other anxiolytics, it acts not at the GABA receptors but in the brainstem; it is a noradrenaline antagonist, controlling anxiety and panic by suppressing the flight-or-fight response rather than promoting general inhibition. It is also reported to be non-addictive.

Sulpiride is an older antipsychotic which is used as an anxiolytic as well, at least in South Africa and the UK. A Google search did not discover this use, but I know a number of people who have been prescribed it, with good effect. It is non-addictive and appears to be effective for most people; but it can produce menstrual problems and lactation, as well as 'paradoxical' reactions. When I took it to boost my sleeping pills during an agitated hypomania I panicked instead of relaxing.

The hypnotics of choice used to be barbiturates, but as these are dangerous and easily used for suicide, they are now rarely prescribed. About the only simple way to get them nowadays is to have an epileptic dog (real, borrowed or imagined)—phenobarbital is a standard veterinary anticonvulsant, and is often dispensed quite freely. The only really effective hypnotics (except for sedating antidepressants like Trazodone or Prothiaden for some patients) appear to be benzodiazepines or similar drugs. The standard practice (reinforced by the package inserts) seems to be to prescribe these only for the short-term treatment of insomnia; but many (most?) depressives, even medicated, have chronic insomnia, and doctors are increasingly prescribing hypnotics fairly open-endedly, often effectively for life. At least this is so in South Africa and much of Europe, less so in the US and UK, both of which have a somewhat nannyish attitude

---

Anxiety Disorder], for example, needs benzodiazepine treatment in the same way that a diabetic needs insulin' (Forrest 1999).

toward potentially dependency-inducing drugs.[34]

It is true that one usually becomes dependent on hypnotics, often developing severe and persistent rebound insomnia on withdrawal, and eventually becoming quite unable to sleep without them. But hypnotics are a true blessing. They help to prevent one of the most devastating of all depressive experiences: waking in the wee hours in a suicidal funk, unable to read or listen to music or do anything except examine your mental innards, staring at the ceiling till sunrise and wishing for death. Being on hypnotics for life is a very small price to pay for avoiding this.

The standard hypnotics are benzodiazepines and three drugs with similar effects. Among the most widely used are flunitrazepam (Rohypnol), triazolam (Halcion) and loprazolam (Dormonoct). The non-benzodiazepines are the so-called 'z-drugs', zopiclone (Imovane, Zopimed, Lunesta in the US), zimeldine (Ambien, Stilnox) and zaleplon (Sonata). All are reasonably effective and short-acting, so one does not end up with much if any of a hangover. They enhance slow-wave sleep, and help provide more restful nights than one would get without them. The CNS and respiratory depressant activity of all these drugs is potentiated by alcohol; whether it is safe to drink while using them is a matter of debate (see the section on alcohol below).

Electroconvulsive Therapy

The idea of 'shock therapy' is horrifying to many people. It carries overtones of the punitive, and memories of portrayals of sadistic behaviour by callous doctors and tough, uncaring nurses. And indeed in certain hospitals this was once pretty much the case, and not all that long ago. This (semi- or fully) autobiographical passage from Sylvia Plath's *The bell jar* (1963:138) probably reflects the popular image:

> Doctor Gordon [...] dragged out a table on wheels with a machine on it and rolled it behind the head of the bed. The nurse started swabbing my temples with a smelly grease.
>
> As she leaned over to reach the side of my head nearest the wall, her fat breast muffled my face like a cloud or a pillow. A vague, medicinal stench emanated from her flesh.
>
> 'Don't worry,' the nurse grinned down at me. 'Their first time everybody's scared to death.' [...]
>
> Doctor Gordon was fitting two metal plates on either side of my head. He buckled them into place with a strap that dented my forehead, and gave me a wire to bite.
>
> I shut my eyes.
>
> There was a brief silence, like an indrawn breath.
>
> Then something bent down and took hold of me and shook me like the end of the world. Whee-ee-ee-ee-ee, it shrilled, through an air crackling with blue light, and with each flash a great jolt drubbed me till I thought my bones would break and the sap fly out of me like a split plant.

---

[34] Restriction to short-term use has recently been made part of the prescribing protocols of NICE (the UK National Institute for Health and Clinical Excellence). This recommendation has been strongly criticised (Capua & Shapiro 2007). The authors note that insomnia is a serious health risk, and that insomniacs have twice the average incidence of car accidents and four times the incidence of depression as the general population. They recommend unlimited use.

I wondered what terrible thing it was that I had done.

Things have changed radically in the ensuing three decades, though one might not think so from films like *One flew over the cuckoo's nest*, which created a great deal of unfavourable publicity. ECT is no longer a form of torture, and is not (in civilised countries) used as a means of 'control' or punishment. In some cases, such as elderly patients with compromised liver and kidney function, it may even be preferable to medication, or the only safe therapy. Because of its quick action it is often used in cases of emergency, such as violent psychotic manias.

The idea of inducing convulsions to treat psychiatric disorders stems from an old observation, capitalised on in the 1930s: that institutionalised psychotic patients who were also epileptic often gained at least temporary symptomatic relief after a seizure.[35] Such observations led to experimental procedures with seizure-inducing drugs, and eventually, as epilepsy was better understood, to the use of electric currents to disturb the brain's own natural activity, and induce seizures whose duration and severity could be controlled. As suggested above, at first, with the brutality often common to early treatment of institutionalised psychiatric patients, the procedure was barbarous and often abused; nowadays it is reasonably safe and no more traumatic than any other treatment under general anaesthesia..

Unfortunately, though ECT is extremely effective in certain cases, we do not know precisely how it works. There are many theories, any of which may be right (or at least are consistent with the observed effects, and what we know of seizures). One is that the seizure as it were 'reboots' various brain systems, by temporarily inducing chaos, disturbing or destroying normal function, and then allowing it to re-achieve its normal set-point—more or less like defibrillation. This is generally believed now to be oversimple.[36] Among the effects that have been noted are: suppression of regional cerebral bloodflow; facilitation of noradrenaline and dopamine transmission and that of acetylcholine and GABA; increased permeability of the blood-brain barrier; and effects on CRH, ACTH, TRH (thyroid releasing hormone), as well as other neuro-hormones such as prolactin, vasopressin, and endorphins (see Bezchlibnyk-Butler & Jeffries 1998: 44ff, Andrade 2008). A lot more research is needed for a clear understanding of why seizures, normally to be avoided, can be so useful in restoring the brain's proper affective settings.

There is no doubt that ECT works well for certain intractable depressions. It is also slightly risky, and may have unwanted side-effects. The risk is not great: two studies cited by the US National Institutes of Health (NIH) show fatalities of 2.9 per 10,000 patients, and 4.5 per 100,000. This is equivalent to the normal risk for any procedure involving general anaesthesia.

ECT is now given under anaesthesia, and the use of muscle-relaxants largely prevents the

---

[35] ECT is not a unique instance of producing major pathology for therapeutic purposes. Radiotherapy and some forms of chemotherapy for cancer do the much the same thing: by killing rapidly dividing cells they get a lot of normal ones along with those from the tumour.

[36] For discussion of the various theories and evidence, as well as an excellent bibliography, see Fink 1997.

fractures and severe muscle pain that used to occur. The main complications run at about 1% of all procedures (based on an NIH sample of 25,000): they include laryngeal spasm, breathing problems, occasional vertebral compression fractures, and very rarely status epilepticus (a potentially fatal continuous seizure).

Recovery of consciousness is usually followed by a period of up to 24 hours of mild to moderate confusion and memory loss, often with accompanying headache. The most severe and persistent problems appear to be associated with memory, but the evidence is contradictory, and it is not clear how many patients suffer major or permanent memory loss, though some certainly do. There is one strand of opinion that considers the memory effects often to be major and permanent, and much work has been done on finding ways to improve memory deficits (Andrade 2008). It has also become quite fashionable (as it is with antidepressants as well) for some people who have had bad experiences to describe themselves as 'survivors' and become anti-ECT advocates. Some of the literature suggests that major and permanent memory loss is not infrequent; on the other hand, some clinicians I have spoken to have precisely the opposite opinion. Given my profession, with its critical dependence on high-functioning memory, as well as the evidence in the literature, if I were offered ECT I would refuse it, just on the off chance.

At one time ECT was used for a very large range of conditions (e.g. schizophrenia, other delusional psychoses, catatonia); nowadays its use is much more restricted, and it seems to be most effective in delusional or very severe melancholic depression, or acute mania—particularly when the disorder has been refractory to medication. It is relatively ineffective for milder depressions or dysthymia. One advantage of ECT in really severe cases is that the onset of therapeutic effect is a good deal faster than with medications. The reported results are generally good: according to the NIH, 'not a single controlled study has shown another form of treatment to be superior to ECT in the short-term management of severe depressions', and it is at least as effective as TCAs, more effective than MAOIs, and about as effective as (and faster than) lithium for acute mania. But there is a lack of long-term studies as ECT is normally followed up by medication, and it commonly has to be repeated, often quite regularly.

The procedure is still in some ways controversial; it is sufficiently invasive and ill-understood so that it ought to require special discussion and both ethical and medical care in its administration.[37]

[37] For a recent survey and meta-analysis see UK ECT Group 2003.

Self-Medication

> He mentioned to me how, for the first time, that he had been distrest by melancholy, and for that reason had been obliged to fly from study and meditation, to the dissipating variety of life. Against melancholy he recommended constant occupation of mind, a great deal of exercise, moderation in eating and drinking, and especially to shun drinking at night. He said melancholy people were apt to fly to intemperance for relief, but that it sunk them much deeper in misery.
>
> —James Boswell, *Life of Johnson* (1791)

Humans have probably been taking psychoactive chemicals since they discovered that plants had uses other than food. By the late Bronze Age we have evidence for the use of hallucinogens like *Cannabis*, the fly-agaric mushroom (*Amanita muscaria*), and members of the *Solanaceae* (tomato family): e.g. *Atropa belladonna* (deadly nightshade), *Hyoscyamus* (henbane) and *Mandragora* (mandrake). The psychostimulant properties of *Ephedra* may have been known to the Neandertals (there are remains of its pollen in the 50,000 year old burials at Shanidar cave in Iraq), and opium has been in use in Europe at least since 4000 BC.[38] My concern in this and the following section however is exclusively with two of the most widely used (and legal) psychotropics: alcohol and nicotine. I restrict myself to these because I know them from personal experience; and because, perhaps wimpishly but in the end it turns out wisely, I happen never to have taken illegal street drugs (except for cannabis a few times in my 20s). This is due initially to the behavioural style of the time and society I grew up and lived in, and later to having learned enough to know that cocaine, amphetamines, Ecstasy and hallucinogens are extremely dangerous for people with mood disorders.

Many, perhaps most depressives have been smokers, drinkers, and/or druggies of other kinds, long before they ever get to a doctor and have anything prescribed. Many indeed never do, and end up perpetually miserable or dead, or manage to hang in there with pretty poor quality of life, or even be compromisedly or periodically happy, on these rather dodgy chemical support systems. My personal and controversial view is that alcohol and nicotine may, for some, have benefits that come close to matching their undeniable and serious dangers. In any case, they are so widely used as palliatives for bad moods that they have to be discussed.

---

[38] For discussion and references, see the relevant entries in Rudgley 1998. Except for cannabis and opium and some of its derivatives, most of these are no longer 'drugs of abuse'; but some of our most useful medications (e.g. atropine) are derived from or synthesised after the classics. Ephedra itself is not used for medical purposes, but a synthetic relative of the active ingredient (pseudoephedrine) is one of the commonest and most effective decongestants. Unfortunately in many countries it is now unavailable or available only in limited amounts by prescription, because it is a precursor in the illegal manufacture of methamphetamine.

Alcohol

> I lived, I loved, I quaff'd, like thee:
> I died: let earth my bones resign:
> Fill up—thou canst not injure me;
> The worm hath fouler lips than thine [...]
>
> Why not? Since through life's little day
> Our heads such sad effects produce;
> Redeem'd from worms and wasting clay
> This chance is theirs, to be of use.
>
> —Byron, 'Lines inscribed on a Cup formed from a Skull'

Alcohol, despite its delights, is potentially highly toxic, particularly in the long term. It raises gastric acidity, conducing to or exacerbating oesophagitis, gastritis and ulcers; it can damage cardiac muscle, cause hepatitis and cirrhosis of the liver, pancreatitis, peripheral neuritis, brain atrophy, and is at least statistically implicated in oral and oesophageal cancers. It can induce blackouts and eventually total and permanent amnesias. Less dangerously, it can also cause erectile dysfunction ('brewer's droop').For the addicted, withdrawal can lead to delirium tremens and in some cases death. In addition, and this is of significance for patients on psychotropic medications, there are some potentially dangerous interactions. Certain anticonvulsants (especially valproate) can increase intoxication, the absorption of Prozac can be increased, as can the depressant effects of TCAs and benzodiazepines. And this of course aside from its social effects: the dangerous and violent behaviours it can trigger through its disinhibition of the frontal cortex.

The Bible is quite properly ambivalent about alcohol. The Book of Proverbs says: 'Give strong drink unto him that is ready to perish, and wine unto those that be of heavy hearts. Let him drink, and forget his poverty, and remember his misery no more'(31:6-7). On the other hand (20:1), 'Wine is a mocker, strong drink is raging: and whosoever is deceived thereby is not wise'. Alcohol is one of our earliest psychoactive discoveries: we have been using it for at least the past 10,000 years. It has been discovered and rediscovered time and again, not only as a psychotropic but as a food (particularly beer).[39]

It is well known that the proportion of depressives who are serious or excessive drinkers is much higher than in the population at large. The direction of causality is unclear: does

[39] For a fascinating account of the history of alcohol use, see Vallee1998. The best book I know on both the good and bad sides of alcohol is the English wine writer Jancis Robinson's *On the demon drink* (1988). Some of the medical information is a bit out of date and there are a few inaccuracies; but it is beautifully and amusingly written by a connoisseur with considerable balance, and worth reading by both drinkers and temperance campaigners. For a short, highly technical but informative introduction to the psychopharmacology of alcohol and the treatment of alcohol dependence, see Schuckit 2000. For an immensely detailed account of the action of alcohol on all brain systems see Oscar-Berman & Marinkovič 2007.

depression cause heavy drinking, or is it the other way round? Or both? Many depressives drink a great deal, and many alcoholics and alcohol-dependent heavy drinkers (I will distinguish these categories later) have mood disorders. The existing studies appear inconclusive, but there are repeating themes, and evidence for causality in both directions. Pre-existing alcoholism is associated with mood disorder: according to one literature survey somewhere between 12% and 57% of alcoholics have affective illness. This is only for alcoholism, not for 'alcohol abuse' (assuming the two terms really mean something different: I will return to this issue below), but it is suggestive (Goodwin & Jamison 1990: 213). There are also indications of a genetic link between alcoholism and manic depression and other mood disorders.[40]

The immense mass of studies provides varying but more or less convergent results. In a group cited by Goodwin & Jamison, the rates of above-usual drinking ('alcoholism', 'problem drinking', 'drinking to excess', 'abusing alcohol'), ranged from 25%-75% of target groups of patients 'with mood disorders'. The population incidence of alcoholism in the non-depressed in the US appears to be around 8%.

While there is no doubt a strong connection between mood disorder and heavy drinking, the literature makes it very difficult to see what precisely is going on—largely because of non-comparable survey populations and lack of uniform definitions. The latter is especially troubling: what is an 'alcoholic', as opposed to someone who is merely 'alcohol dependent', 'drinks to excess', has 'drinking problems', or 'abuses alcohol'? What counts as 'excessive' or 'heavy' drinking is unfortunately a matter of local medical fashion: at present the standard South African and US definition of a 'heavy drinker' (male: the limits for women are somewhat lower) is someone who has more than two drinks a day, while in Canada even 7 drinks a week is considered 'dangerous', which is alarmist to the point of paranoia. Other countries, according to a survey in *The Independent* (19 May 2008) have rather different standards: in France the danger point comes at 5 drinks a day, and in the Basque country the approved limit is one drink a day per 12 kg body weight. This is not science but cultural predilection. For clarity I stipulate that all alcoholics are by definition alcohol-dependent, but not vice versa. I reserve the term 'alcoholic' for the real 'problem drinker', whose family life, relationships and work are interfered with by drinking, who gets into trouble with the law, has blackouts, virtually devotes his life to obtaining alcohol and drinking and exhibits the kind of uncontrolled behaviour typical of late-stage addicts.

On the other hand, there is what I would call the 'non-alcoholic alcohol-dependent'. I classify myself this way (and so does my psychiatrist). I drink a good deal, every day. At a certain time (after about 15 hours of abstinence) I usually feel that I need a drink, and may suffer withdrawal symptoms (anxiety, tremor, depression) if deprived. I am normally quite unable to get to sleep sober, even with sleeping pills. So I am dependent, even addicted, but not 'alcoholic' in the problematic sense. I do not drink before going to work, or during a working day when not at home, except perhaps a glass of wine or a beer with lunch, and a whisky or two around 3 PM,

[40]For anxiety disorders, which are closely related to depression, the available data seems to indicate that the psychiatric disorder tends to precede the drinking disorder: see Crome & Bloor 2008.

or perhaps one before a lecture if I happen to have a bad anxiety attack. Drinking does not interfere with my relationships or productivity, I do not devote time to it that would be better devoted to other activities, I never drive when drinking or otherwise get in trouble with the law. And I am rarely actually drunk except when it is appropriate, e.g. at social events or parties or spending evenings with friends.

Why should there be this relationship between heavy drinking and depression? Alcohol is a central nervous system depressant: you pass out when you drink enough. Why then should it be a drug of choice for the depressed? The oversimple answer is that it is the only cheap, legal and potent psychoactive drug that you can get without a prescription in most western countries, and in the fog of severe depressive (or manic) states, just about anything that will do something to your head is worth trying. But the real story is rather more complex.

Alcohol is indeed eventually a depressant; many depressives who become heavy drinkers begin by using it to ward off intolerable insomnia (it does, but you pay for it with disturbed sleep), or simply to get rid of consciousness for a while. Any regular sufferer of hangovers will know the dreary mood that often accompanies, but is not entirely caused by, the headache, nausea, furry tongue and staggers of the morning after. But it is also the recreational drug of choice for those not into the drug-culture; it oils the wheels of conversation, makes people (either really or in their own imaginations) cleverer and more fluent than they would be without it. Conversation always seems to flow better at table when quantities of wine are consumed than not, and pubs are particularly fine places for talk—even serious intellectual talk (I have always thought of Oxford and Cambridge as networks of pubs with a superstructure of colleges). On the other hand drunkenness often leads to aggressiveness, violence, hypersexuality, inflated self-esteem, risk-taking behaviour—actions and attitudes associated with mania rather than depression. So despite the ultimate depressant effects, alcohol can also provoke states rather more like hypomania or mania.

What then of the manic depressive who drinks, not just in ordinary social situations or to relax at the end of the day, but at least partly for control of mood? Aside from drinking regularly just because I really adore good whisky, beer and wine, and am physically dependent, I drink when I am depressed, and often get temporary relief through elevation of mood and a pleasant feeling of irresponsibility (conveniently suppressing the knowledge that the depression may get worse later). I drink when anxious, because alcohol is the fastest-acting anxiolytic I know. But I also drink when manic, and for two opposed reasons: for relief from rage, agitation and panic in black manias; and contrariwise to prolong or enhance the euphoria of good hypomanias.[41] Alcohol is a complex and paradoxical drug, with an extraordinary range of effects.

There are three interconnected actions it is best loved for. In the initial stages it

[41] The latter behaviour is characteristic of cocaine users as well; despite the fact that cocaine is a potent psychostimulant, bipolar patients report using it more when manic than when depressed, as a secondary euphoriant to enhance the up state (Goodwin & Jamison 1990: 217f.). Many manic depressives find their highs as addictive as any drug, and anything that works to prolong them becomes an important part of their armoury of weapons against the life they would otherwise lead.

antagonises the inhibitory neurotransmitter GABA. This leads to suppression of normal higher-cortical (frontal lobe) controls, and thus to disinhibition, mild euphoria and freedom from social and behavioural constraints that might otherwise operate. Second, and here is where the possibility of dependence begins to arise, alcohol promotes the release of dopamine in the limbic 'reward centre'. And third, it also stimulates limbic opiate receptors, contributing to a general feeling of well-being, often, in just the right quantities, something like hypomania. Its initial effect therefore can be (and usually is) antidepressant, anxiolytic, and euphoriant. But it also interacts with the serotonin system, which may lead (unpredictably, depending on the individual) to a range of behaviours, some tolerable, others dangerous or even fatal.

Alcohol does many other things, and the more you consume the more dangerous and disabling these may become. From the outset there is some cerebellar inhibition, leading to increasing lack of coordination. There is also a growing impairment of judgement. Later in the course of consumption there is a kind of 'rebound' effect, where the stimulation is undone, and suppression of activity in the hippocampus, which affects memory. (The extreme version is the alcoholic blackout; the final result may be a devastating amnesia called Korsakov's syndrome.) Excessive intake can lead to respiratory depression and death.

Alcohol, like most psychoactive drugs, is very personal; anyone who has observed enough drunks knows that some become maudlin and weepy, some flirtatious, some merely more fluent and charming than when sober, some incoherent, others aggressive and dangerous. This may in part be due to its effect on the serotonin system. Because of serotonin's link to status and dominance, dysregulation can precipitate violence in vulnerable people. The combination of pleasure, loss of coordination and defusing of cortical inhibition (and hence loss of judgement) can make alcohol an exceedingly dangerous drug for the wrong people; for the right ones it can make it a key to enhanced quality of life.

The use of alcohol along with other psychotropics is generally not recommended. Most antidepressants (and tranquillisers and hypnotics) come with a warning either that alcohol is to be avoided, or should be 'used with caution', because it may, among other things, potentiate CNS depression. How seriously should dedicated or dependent drinkers take these warnings? As usual, the answer is 'it depends'. On the state of your liver, how badly alcohol affects you and in what way, how much you need it, what other drugs you are taking, and how strong the interaction (if detectable) is. I would probably be somewhat less depressed (and would certainly have less gastritis and perhaps lose some weight) if I drank less; on the other hand, the stress incurred through the loss of a fundamental pleasure, additional anxiolytic, euphoriant and comfort might itself make me worse. My use of alcohol is not only palliative and addictive, but hedonistic, which may be useful in depressive disorder. The books do not usually list it, but simple pleasure can be potently antidepressant (at least if you are not so depressed as to be immune to it).

The manufacturers of two activating antidepressants (Aurorix and Effexor) specifically say that there is no interaction. But there is one, Wellbutrin, that can occasionally lower alcohol tolerance, at least to the degree of provoking quicker drunkenness and dreadful hangovers in some patients. *Depressant* drugs (tranquillisers, sleeping pills, etc.) are another story entirely; but even

then for some there is no apparent problem. Package inserts are not an accurate guide in these matters: unfortunately the only way you can find out is to try yourself (*very* carefully at first) and see what happens. But this can be dangerous. I have drunk fairly heavily for a decade and a half (about 3 litres of spirits a week plus a certain amount of beer and wine) while taking benzodiazepines and sleeping pills, and many of my depressed friends likewise, and/or with sedating antidepressants. None of us appear to suffer any functional deficits; but it would be irresponsible to recommend such mixtures. So many people have idiosyncratic reactions to drugs, and mixing alcohol and benzodiazepines (which has turned out to be safe for me—so far) can lead to respiratory depression and death. I seem lucky enough to have the right constitution for the behaviour I want to indulge in. But I only found that out though experimenting, with no idea of or particular concern for the consequences—typical depressive behaviour. I simply could not conceive not drinking, and considerations of risk took second place. It fortunately turned out this was all right for me. Mixing alcohol and *any* depressant (benzodiazepines, sedating antidepressants, opiates, mood stabilisers) is at least risky, and it is better to avoid it if you can.

The only consequence I have seen so far is disordered sleep and something of a hangover most mornings. But this is what *I* choose to do, not a suggestion for anybody else. It may well be ignorant and misguided, and almost certainly involves an element of deliberate risk-taking. (It may also not even be what I 'choose' to do, but simply a surrender of my autonomy to the pleasure and the addictiveness of a drug.)

Tobacco[42]

> You are my Gypsy, my spouse, my man; I am your Gypsy, your spouse, your woman. Marriage to Carmen, like that of a smoker to his cigarette, is eventually fatal, but it embraces an impossible idea, a gauzy ideal of hymeneal union—marriage that combines the most exhilarating perspectives on freedom with the most irrefractable bonds of habituated pleasure.
>
> —Richard Klein, *Cigarettes are sublime* (1993)

Nicotine itself is probably not a dangerous drug;[43] what is dangerous is using tobacco. This is not a paradox; it is because (except in the case of preparations used to help in smoking cessation) one does not typically encounter pure nicotine. What one smokes or chews or inhales is the entire leaf of *Nicotiana tabacum*, a complex living organism; and this is full of bioactive chemicals

[42] For a thorough and accessible account of just about every aspect of smoking—historical, social, pharmacological, medical, see Ashton & Stepney 1983. This is a marvellous book for the smoker and the non-smoker, both of whom will emerge better educated, with many of their prejudices reinforced, and will learn a lot about how smokers start and why. For a detailed medical overview, see Swan & Lessor-Schlaggar 2007.

[43] Actually it is dangerous in large quantities if ingested; extracting the nicotine content of a pack of cigarettes and consuming it would kill you. It was popular, especially in the 19th century, for poisoning members of the family, as it is the easiest toxic alkaloid to get hold of without having to visit a chemist or any other place where your purchase would be noted.

already, in its unburnt state. But combustion of the dried leaf produces a huge number of additional toxic and carcinogenic substances: among them carbon monoxide, cyanides, arsenic, cadmium, formaldehyde, ammonia, phenol, toluene and butane—altogether some 4700 substances have been identified so far (Swan & Lessor-Schlaggar 2007).

Smoking is a dangerous habit. It is unfortunately also mood-enhancing and hugely pleasurable to many who engage in it (though some smoke only out of addiction and do not really enjoy it).[44] It greatly increases the risk of cardiovascular disease, obstructive airway disease, chronic bronchitis, and cancers not only of the lung, but of the oral mucosa, larynx, oesophagus, stomach and bladder. At a slightly less dramatic level it can produce, at least in heavy smokers, shortness of breath, coughing, wheezing, chronic upper airway irritation, sinusitis, gastritis, raised blood pressure and erectile dysfunction; it also exacerbates the formation of tartar and therefore dental decay and gum disease.

Tobacco was probably known in the Americas as a recreational and/or ritual drug for millennia; but its introduction to Europe dates to the early 16th century, after the opening up of the New World. It was probably brought from Portugal to France and thence to the rest of Europe by the French diplomat Jean Nicot (1530-1600), after whom the plant (*Nicotina*, later *Nicotiana*) and its alkaloid were eventually named. Ashton & Stepney (1983:1) call it 'The Indian's Revenge', and note:

> We derive our knowledge of tobacco from Columbus. The finding of the enchanted weed must rank somewhere between the introduction of syphilis and the discovery of America in terms of the ultimate benefit to mankind of the consequences of his stubborn voyaging.

This seems a reasonably sound appraisal, though never having had syphilis I can't be sure. But there is no doubt that smoking is widespread and important to its practitioners (or victims if you prefer), and that the main psychoactive component of tobacco smoke is nicotine.

The pharmacology of nicotine is complex. Like alcohol, it has two apparently antagonistic effects: stimulant and sedative/anxiolytic. It (temporarily) acts as an agonist at certain acetylcholine receptors in the brain (the two molecules are almost identical in shape), and produces a relaxing effect by inhibiting the sympathetic nervous system. It promotes dopamine release, the *sine qua non* for pleasurableness (and addictiveness). It also releases β-endorphin, an endogenous opioid which produces feelings of calm and relaxation, and itself stimulates dopamine release, so the limbic pleasure centres get a double dose (Pontini *et al.* 1996). On the other hand, it produces alertness and stimulation by raising serum glucose, adrenaline and cortisol levels. Nicotine is also a weak MAOI, which adds to its antidepressant, euphoriant and anxiolytic effects (Fowler *et al*. 1996). There are extensive psychological benefits obtainable

[44]There is a strong correlation between smoking and mood-disorder, and the results of various studies suggest strongly that smoking is used therapeutically. In one US survey of psychiatric outpatients, over 50% were smokers, which is twice the non-depressed population average (Acton *et al.* 2002). In a study of smoking cessation (Anda *et al.* 1990), smokers who presented at initial examination with depression were 40% less likely than the non-depressed to have given up when re-examined 9 years later.

from this ambiguous drug; though apart from addiction and raised blood pressure, the real dangers are rather from the chemicals nicotine co-occurs with in tobacco.

Nicotine (or perhaps more accurately smoking—see below) is highly addictive; withdrawal can be epically unpleasant, and is often unsuccessful. Judging by my own attempts, the withdrawal syndrome may include depression, suicidal ideation, agitation, irritability, rage, paranoia, anxiety verging on panic, nausea, insomnia and tremor.(And this while drinking fairly heavily and taking antidepressants and benzodiazepines.) Of course it is a very good idea never to start smoking; any idiot knows that. For smokers it is a physically healthy act to stop. On the other hand smoking—certainly in my case—can be a useful if dangerous and physically destructive adjunct to the overall palliation of mood disorder. There is no doubt that smoking, like drinking, has been an important and at least psychologically 'healthy' part of my life. It produced useful and delicious and potent effects, and helped make my condition easier to bear.[45]

I close with a little, perhaps to some eccentric and dangerous, excursus on aspects of smoking and smoking cessation which are typically not considered in the medical and pharmacological literature. This often causes discussions to miss the point of why withdrawal is so difficult, at least for certain smokers. I take myself as an example, since I am wrestling with this at the moment. For me (and this is not unusual) it is not just a matter of pharmacology. Though stopping smoking, and at least largely controlling the pharmacological addiction was horrible and painful enough, it was by no means the only significant part of the trauma of cessation.There is a further complication. Yes, the nicotine craving is still there periodically and unpredictably, and I can always take nicotine replacements when it recurs, and they help a bit to control it. But what is really unspeakably awful is not just the lack of nicotine, but the sheer nostalgia and almost amorous longing for the *act of smoking* itself and its accompaniments: the taste, the scent of tobacco both combusted and uncombusted, the way it begins to glow on lighting, the delicate formation of the ash, the endless fascination of smoke curling up into the air, the lovely bluish grey tobacco smoke takes on in certain lights, the incredible variety of flavour (Cuban vs. American vs. English vs. East Indian vs. Turkish ...), the feel of the cigarette in the

[45]Covey *et al.* 1997 evaluate the risk of major depression following giving up. In patients with no prior history of depression, the risk was low (2%); with a single prior major depressive episode the risk was 17%; and people with histories of multiple episodes had a 30% incidence of new ones. This again suggests that a balancing of risks is useful, and that simply getting depressed patients to give up may not be the best medical strategy. The smoking/depression connection seems to be very complex indeed; there is now some evidence for a genetic predisposition for nicotine-dependency, and the current 'candidate genes' for this predisposition are concerned with dopamine uptake and metabolism of nicotine (Branch 1999). Another study shows an apparent positive correlation between 'negative childhood experiences' (physical, sexual or emotional abuse, having a battered mother, separated or divorced parents, substance-abuse or mental illness in the family) and beginning to smoke at a young age and continuing (Anda *et al*. 1999). Smokers, according to this study, were 'always more likely to be depressed for any given level of exposure to adverse childhood experiences', which may suggest early ('naive') self-medication, and perhaps a connection with the genetic mechanisms for vulnerability to mood disorder..

hand, the harsh but exquisite plunge of smoke into the trachea ...[46] That is all still there in physical memory, and missing it is probably the worst part, perhaps even worse than the actual nicotine withdrawal. If anything makes me return to smoking (even having finally got emphysema from it) it will be the loss of this part of my life rather than just addiction to the drug. I did not realise before giving up how many senses are involved in smoking, and how (for me and many others I know anyhow) the pleasure is so overwhelmingly intense, and distributed over so many modalities. So in stopping I am depressed and angry and sadly nostalgic not only because of withdrawal from nicotine, but because so much of my most vivid and delicious sensory life is gone. And at least in my experience so far, this part of cessation does not get better.[47] So although medical opinion would (quite properly from the purely physical point of view) say 'stop!' without further reflection, there is for some addicts, especially the mood-disordered, something to be said for continuing—as long as one is both fully aware of the risk, and willing to take it.

Dependence

> Dans ce monde étroit, mais si plein de dégoût, un seul object connu me sourit: la fiole de laudanum; une vielle et terrible amie; comme toutes les amies, hélas! féconde en caresses et en traîtrises.[48]
>
> — Charles Baudelaire, *Le spleen de Paris*

Many people object to taking psychoactive drugs out of fear of 'dependence' or 'addiction'. Terminology in this area is rather muddled, and it is not at first entirely clear what the distinction is (though there certainly is one) between 'pathological' addiction and ordinary garden-variety dependence. I will avoid the colloquial terminology for the moment, and look at some of what *DSM-IV* has to say about 'Substance-related disorders', a hugely complicated set of categories. A useful distinction can perhaps grow out of that. 'Substance Use Disorders' (e.g. dependency and 'abuse') are distinguished from 'Substance-Induced Disorders' (intoxication, withdrawal,

[46] If this and the description below seem rather purple and overwrought, look again at the epigraph to this section and read the book it comes from. What I say here is rather mild. There is just something different about smoking, especially cigarettes. A friend of mine remarked recently that cannabis and alcohol for instance are just drugs, but a cigarette is a friend. I understood immediately what she meant and missed them even more.

[47] The distinction between the two facets of addiction is very clear from my behaviour.If I just need a shot of a drug, a purely physical need, I can smoke the most awful cheap cigarettes or drink the crappiest blended whisky. This gets rid of the immediate chemical craving, but is neither satisfying nor any response to the other kind of longing. If I have an expensive cigarette or whisky, of really good quality, then the chemical need gets taken care of and there is the extra, the aesthetic, too. And if I have no particular need for alcohol, say, at a particular moment, I will often still have a glass or two of Lagavulin or Highland Park the same way and for the same reason as I would eat an expensive piece of Swiss or Belgian chocolate (which I am not at all addicted to): just because it tastes so lovely. And loveliness is not a prominent part of the depressive world.

[48] 'In this constricted world, so full of disgust, one sole familiar object smiles at me: the vial of laudanum; an old and terrible friend; like all friends, alas! rich in caresses and treacheries'.

etc.) Dependency then is in the *DSM* framework itself a 'disorder', on a par presumably with Bipolar Disorder or Major Depression. So, considering my use of both prescribed drugs and self-medication, should I also be diagnosed with yet another disorder on top of my Bipolar II? Dependence is defined as a 'maladaptive pattern of substance use', whose signs are at least three of the following: (1) 'tolerance' (increased need for the substance); (2) withdrawal symptoms on stopping; (3) presence of persistent (ineffectual) desire to cut down or stop; (4) reduction of social activities to spend time using the substance; and (5) continued use 'despite knowledge of [...] a persistent or recurrent [...] problem that is likely to have been caused or exacerbated by the substance (e.g. [...] continued drinking despite recognition that an ulcer was made worse by alcohol consumption)'. This definition of course does not apply to use of prescribed medications, unless 'drug-seeking behaviour', such as going to different doctors for multiple prescriptions, becomes part of the clinical picture.[49]

If we try and fit this into everyday usage, meeting all the criteria would not be what might be called 'benign' dependency, but rather'addiction'. In a listing of all the substances I currently take, a rather complex picture emerges, with different profiles for different ones. I here include both prescribed and 'recreational' substances (the numbers refer to the *DSM* criteria mentioned above):[50]

`

Criteria	1	2	3	4	5
Effexor		x			x
Fluanxol					
Alprazolam		x			
Zopiclone		x			
Tobacco	x	x	x		x
Alcohol	x	x			x

Note that (4) is the only criterion I never meet. My smoking and drinking clearly qualify as substance-use disorders; though there is a slight diagnostic problem in that the category of tolerance is no longer 'active'. I must long ago have increased my tolerance to both, to get to where I am now; but this is so far in the past that I could no longer be said to have (increasing) tolerance in the active sense, but only to 'be tolerant' as a steady state. I have not increased the amount I smoke and drink for at least twenty years. Effexor and alprazolam both induce withdrawal, but in rather different ways, at least from a psychological point of view. Many

[49] It must be noted that all the symptoms listed here are part of the definition only of dependency; 'abuse' is quite different, and the *DSM* uses it to mean recurrent use that causes one to fail to meet obligations, use in hazardous circumstances (e.g. driving), use causing legal problems, or persistent 'social or interpersonal problems'. However much I drink, for instance, I am apparently never, by this definition, an abuser. Which presumably = 'alcoholic' .By these criteria I suspect it is not possible to be technically a nicotine abuser.

[50] I appear to have given up smoking, but I include it to capture the picture that occupied such a large part of my life.

antidepressants produce some kind of 'discontinuation syndrome' when you come off them, but of course they are not taken to induce pleasure in the first place; most do the opposite. And the physiology is different from that of withdrawal from addictive substances. Alprazolam is ambiguous, since I not only take it for its prescribed effect, but actually happen to enjoy it, so even though it is prescribed for a definite medical end which it accomplishes, it is in some ways rather more like tobacco and alcohol. Especially in the sense that if it were to be made illegal (and here I think I have finally hit on the best definition so far of true addiction) I would undoubtedly hunt it up on the street and be willing to pay exorbitant amounts for it and risk arrest. The same is probably true of zopiclone, though here the result is not so much what one would call 'pleasure' as the simple ability to go to sleep. Under the same circumstances I might not go looking for Effexor or Fluanxol—until my depressions got too bad. And the same would be true of alcohol, and cigarettes if I happened to be smoking at the moment.

Certainly with respect to tobacco and alcohol I am diagnosable with a disorder; with respect to alprazolam and zopiclone I am not, but I think should be from a functional point of view. While the *DSM* classification lays out the possibilities clearly, it does miss certain points with respect to the degree of distress caused by withdrawal. It is possible according to the *DSM* criteria (and my personal ones) to have a substance use disorder but not be an abuser. 'Abuse' is an extreme subcase of dependence or addiction. In the most restrictive and useful sense, an addiction (to alcohol, tobacco, cocaine, gambling, eating, sex, the internet ...) is a *compulsion* to engage in some rewarding behaviour. A compulsion may change over time: (a) the craving may strengthen (alternatively, the addictive item becomes less effective), which leads to increased seeking of the drug or activity in question; (b) withdrawal of the object of addiction causes increasing physical or psychological distress, even to the point of being disabling or lethal; and (c) the behaviour leads to social or other dysfunction, e.g. interferes with work or relationships, or provokes violent or other antisocial behaviour, like stealing to get money to satisfy the addiction. In extreme cases the addict virtually lives only for the addiction, like the classical end-stage junkie. This is the far end of the dependence scale (more or less what *DSM* would call 'abuse'). 'Benign' addiction, an odd term that I nonetheless like, is one in which the craving does not strengthen over time, and the dependence does not lead to dysfunctional living—except in the sense that dependency itself may be considered by some to be a dysfunctional state. Rather than being numerical the difference is qualitative: it is *particular* features that count, not the number of them.

Can it be all right to be an addict?

I would even claim essential harmlessness for many addictions, at least for certain personality-types. As should be clear by now, I am what might be called a 'chemical person': if I am in discomfort I am rarely if ever interested in working at finding out the source of the discomfort and perhaps changing my way of living to prevent it; rather I go directly for a palliative drug. This is the vantage-point I write from.

Addiction (in the sense of physiological dependence) is often misconstrued as a moral issue. It is not, or at least does not have to be. For instance, I take alprazolam to reduce anxiety and prevent panic attacks, and offset some of the agitation produced by antidepressants, which it does very effectively. And besides this I enjoy it for its mood-brightening effects, and just the way it makes me feel in general. But I am also addicted to it. If I wait too long between doses I get severe withdrawal symptoms (dysphoria, tremor, anxiety, panic); and if I had to stop cold-turkey rather than following a delicate withdrawal schedule the results would be horrific. But so what? The knowledge that I am addicted in this sense simply does not bother me: I do not spend my days taking alprazolam fixes, I have not increased my dosage in years (though in particularly stressful situations now I do take the odd extra tablet), I have never mugged anybody for alprazolam-money. If the puritan wants to consider this a kind of weakness, let him; for me it is good sense, with a bit of a disadvantage if I happen to run out on a weekend. But even if it turned out that I developed tolerance, and started having to take more and more to keep myself 'normal', showing some classical signs of more serious addiction, but without behavioural complications, there would still to my mind be no problem (except the expense, and the possible danger of eventual oversedation). So on closer examination, given my kind of personality, even an addiction with unpleasant withdrawal symptoms can contribute to quality of life.[51] If that is, the addiction, like mine to alprazolam, alcohol and tobacco, is not merely negatively 'medicinal' (in the sense that the only reason I take these substances is to avoid withdrawal syndromes), but positively pleasurable.

In many addictions (or for particular addicts) there is a strong element of habit. I know that I am physically addicted to nicotine, and I know the chemistry that says why; but there are times (paradoxical as it sounds) when I need a cigarette even though I don't need one. Like when sitting down at my computer, having a cup of coffee or a drink, talking and drinking with friends (those few who still tolerate my smoking). These largely routine-induced acts might be called 'habitual' addiction responses rather than 'necessity' ones. I am at the moment of writing not smoking and given the state of my lungs will most likely not start again; but for information the description here is of the smoking me. (I can probably be accurate, since in no way do I think of myself as a non-smoker. I am a lapsed smoker for health reasons, but except for not performing the activity my psychological state is more or less unchanged.) These habitual responses are the most controllable; I generally know, for any cigarette or drink, which category it comes into, and if I

[51] My (undepressed and fit) friend M comments, and quite properly: 'The difference in attitude is because you live with a chronic debilitating disease. Many/most other people don't. Their attitude is the logical converse of your attitude toward undermedication of your condition because you don't want to be pharmacologically disabled. [See the following section] To people for whom being relatively healthy is the norm, illness or pain signals malfunction of the system. People like to be in control and malaise may indicate the desirability of a number of changes: in diet, exercise, life-style or other behaviours.' Indeed, for some. I might add that as depression in particular stabilises, the motivation to feel healthy also tends to increase, if very slightly. But this motivation may conflict (as it does in my case) with depression-induced passivity and a love for the addictive substance so powerful that one feels unenthusiastic about the benefits of withdrawal, or the never-experienced or long-forgotten pleasures of good health.

feel I am having too much of either I can (much of the time) control these fairly well.

There is also the purely hedonistic aspect, the 'luxury addiction-response'; the drug is taken on occasions which are neither necessary nor habitual. These (*luxuria* 'lust' is one of the Seven Deadly Sins) are deeply pleasurable, and this itself is a contributor to mood elevation. Dependence or not, there is a potent aesthetic component to an ambrosial substance like a fine malt whisky that would not be satisfied by raw spirit.

Addictions like mine to alcohol and tobacco have their costs—aside from the physical damage they do, which goes without saying. A certain vigilance is required: a cache of extra cigarettes, a sure source of booze. When travelling I have taken to carrying a traditionally Victorian-looking pewter hip-flask in my coat-pocket as a kind of security blanket, if I go anywhere that I will be unlikely to find a bar precisely when I need one. I have a potently dreary memory of sitting for hours on the squalid platform at Peterborough station with the East Anglian wind whipping old crisp-packets about my ankles, the buffet closed, no way of getting anything to drink, waiting for a train that never seemed to come. Never again. And even the flask itself adds a dimension of eccentricity and archaic tradition that is its own source of mild pleasure. One might say of addicts like me what W.S. Gilbert said of villains in the *Pirates of Penzance*: 'Their capacity for innocent enjoyment/Is just as great as any honest man's'.

In the end it appears to me that there is only one question that really needs answering, and I have my own answer to it, though others may disagree. Why should one suffer distress if there are substances available to prevent it—regardless of whether they happen to be dependence forming or even addictive? Some people just object to 'taking pills', through what Peter Kramer calls 'pharmacological Calvinism', and even exhibit a perverse pride in the stoicism displayed by suffering needlessly from headaches or indigestion or other ailments. This attitude strikes me as irrational and counterproductive at best, and at worst a perverse self-aggrandisement, a fake machismo or self-induced martyrdom. (I do not understand or have any sympathy with martyrdom or self-imposed suffering either, but that may be my own limitation.) I will however deal below with a related matter: the possible utility of certain kinds of suffering in particular circumstances, and the potential downside for certain patients of really effective treatment. All in all, it is better to get rid of a disease, or at least mitigate it, than to suffer it because of fears of addiction or dependency, or a belief that suffering is in some curious way virtuous. Though there are some caveats: I present a more positive argument for voluntary suffering and 'imperfect' treatment in the following section, on quite different, utterly selfish and much less philosophical grounds, and in chapter 6 a slightly different one.

Why one might not want to be 'cured'

The overwhelming psychiatric consensus is that bipolar disorder should *always* be treated with a mood-stabiliser in the first instance, and antidepressants added (sparingly) if necessary. This received wisdom appears in the standard textbooks and most popularizations. But it may be a counsel of perfection, and not everybody wants a 'perfect' result—at least if that means no

moodswings, and in particular, as in my case, no manias. I have discussed this question with a number of experienced psychiatrists, and in each case the response was not the textbook one. Their judgement was that treating bipolar disorder with antidepressants only, using alcohol and benzodiazepines as fine-tuners, as I have insisted on doing, is risky. There is always the possibility of the drug provoking hypomanic or even manic episodes (which I am quite sure has happened to me), and inducing or sustaining rapid cycling. Nonetheless, because I value my better manias, and feel most truly 'myself' in these states, they concurred with, and some even encouraged, my willingness to forego stability and take the risk of hypomania escalating into mania, because this seems to be the *modus vivendi* I have established with my disease, and feels like the proper course for *me*.[52]

My moodswings, even the depressions which I take as a kind of necessary consequence of the privilege of being allowed hypomanias, are my foundation; they are inextricable from what I consider to be my self, cornerstones of identity. Even though this mercurial and unstable temperament causes frequent dysfunction and misery, it also promotes superior function, and this is not something I want to lose. I emphatically do not recommend this to anybody else, though from what my consultants told me and the choices of some of my friends the decision is not all that rare.[53]

Strangely enough, I really do not want *not* to be a manic-depressive. I only want to be a somewhat better controlled one, a more functional one, a less miserable one, with both highs and lows less disabling than before treatment or during ineffective treatment, but not absent; and perhaps with the possibility of actually being happy (or if that sounds hyperbolic, moderately contented) or close to it for reasonable periods. I think I would find it impossible to live without unstable mood and the potential for certain circumstances to trigger the very best I can do; this would not occur in ordinary everyday euthymia.[54] Being manic-depressive is what I am;

---

[52] One psychiatrist, whose brother is bipolar and takes only antidepressants, remarked that a good marriage and good friends can be an excellent 'social lithium'. And a senior neurologist acquaintance said in the same connection that he does not like mood-stabilisers on principle, and thinks that if I know how to use alcohol properly it is probably safer and less likely to cause cognitive damage. These may be nonstandard opinions, but they are both from experienced professionals. Whether I use alcohol properly rather than dangerously and stupidly is another question.

[53] As Ronald Fieve notes in connection with this attitude (1997: 64): 'The practitioner wants what's best for the patient and the patient's friends and family, while the patient wants to protect his or her *hypomanic advantage*'(emphasis original). Fieve is a bit disapproving and 'doctor knows best', but is willing to admit that there are cases where he as a physician would agree to a patient adopting such a strategy.

[54] At least that is what I think. One could argue of course that I only think that way because of my illness, and if that were properly treated I would end up being quite happy without the turbulence that I have grown accustomed to. I doubt it, but it is not impossible; yet I am not willing to take the chance. I am also too old: why mess about with whatever time I have left? On the other hand, many intelligent and creative people feel differently. L wrote as a comment on this section: 'I would give it up for bland stability; my only requirement would be not to know/remember anything of what it was like to be a more complex & varied emotional being—I would want a drug that would make me forget my self. My therapist feels that this would deposit me in the realm of "half alive", I don't think I care & anyway that's a very subjective judgement. My only fear

medication and recreational drugs have so far helped keep me from going off the rails or committing suicide, and enable me to work and be a reasonably effective social being rather than dissipating my hypomanias in silliness or useless anguish and rage. Both the awfulness and potential value of bipolar disorder have been summed up eloquently by Kay Jamison, herself a highly creative and productive sufferer (1993:125):

> In a sense depression is a view of the world through a glass darkly, and mania is a shattered pattern of views seen through a prism or kaleidoscope: often brilliant, but generally fractured. Where depression questions, ruminates and is tentative, mania answers with vigor and certainty. The constant transitions in and out of the constricted and then expansive thoughts, subdued and then violent responses, grim and then ebullient moods, withdrawn from and then involving relationships, cold and then fiery states—and the rapidity and fluidity of moves across and into such contrasting experiences—can be painful and confusing. Such chaos, in those able ultimately to transcend it or shape it to their will, can, however, result in an artistically useful comfort with transitions, an ease with ambiguities and with life on the edge, and an intuitive awareness of the coexisting and oppositional forces at work in the world. The weaving together of these contrasting experiences from a core and rhythmic brokenness is one that is crucial to both the artistic and manic-depressive experience.

I think anyone who has read this far will see that this book itself reflects, is virtually a portrait of, such a temperament. The unpredictable shifts of style and attitude, the mixture of austere reductionism and low comedy, the interpolation of obscene language into somewhat academic discourse, are characteristic (there will be more later). Like them or not, they define a way of living and writing and looking at the world which at least is mine, and despite my instability is not all disadvantageous.[55]

But some doctors, however well-intentioned they are, can be a serious problem. Conscientious ones, naturally and rightly, want the best possible results for their patients; and for many of them 'best' is usually the closest approximation possible to a relatively 'standard' non-diseased condition. In the technical terminology, they are not satisfied with 'response', but want 'remission'; anything less than the complete disappearance of symptoms counts as therapeutic failure. But there are two people involved in the doctor/patient relationship, and it ought to be a relationship, not a one-way imposition of 'therapy'. If you as patient feel that aspects of your disease are a positive benefit, or so integral to the 'real you' that you cannot do without them, then you have the right to argue with your doctor, and ultimately to refuse some or even all of the

---

would be any residual unnumbed psychic stuffing that the drug couldn't dull'.

[55] My attitude may also have some kinship with the romantic conception of certain diseases (e.g. TB and syphilis) as keys to creativity and pathways to otherwise inaccessible parts of the creative mind. The classic case is the composer Adrian Leverkühn in Thomas Mann's *Doktor Faustus* (1947), who makes a kind of 'pact with devil' by deliberately contracting syphilis, so that the eventual cerebral effects of late stage neurosyphilis will free his musical spirit.

recommended treatment.[56] This is a right that many (perhaps most) people do not exercise; there are complex power-relations between doctors and patients, and argument and refusal of treatment can be difficult for those who are not articulate, knowledgeable, introspective, and of a bolshie disposition. But it is worth keeping the possibility in mind. In the case of bipolar disorder, for instance, especially if the highs are not (or very rarely) psychotic, some people just do not want them treated;[57] they prefer to retain their 'hypomanic advantage'. But as long as both patient and doctor are aware of the risks, the decision should be up to the patient.

As an anonymous contributor to a depression newsgroup put it, after going on to lithium:

> I've been stable a little over a month and I miss the euphoria! I miss being creative and free. I miss being witty and charming. Not going to go off my meds, just a feeling a loss of what was before. Wah!

One might wonder whether her treatment is really the best thing for her as a person, rather than a 'case'. Might it not perhaps be better for her to retain at least some of her original distress, and mitigate the sense of loss? 'Health' can sometimes amount to serious deprivation if aspects of one's illness fulfil genuine needs, or are bedrock properties of one's personality.[58] Maybe doing without them, while making for a quieter life, is giving up too much? It is up to the individual to judge. Here is one case of a very serious manic depressive who had terrible manias, with all the classical symptoms, plus taking cocaine. But the destructive effect of being 'stabilised' was at least equally deadly, and she expressed it with a devastating power and sadness. This is an e-mail she sent me shortly after giving up her regime of antidepressant-only and adding Tegretol:

> Tegretol has dullened me; on the up side (is it?), I've had two nights this week sober. The first two nights without drink by choice and not because I'm severely, painfully hungover, in over a year. I have yet to decide whether or not this is good for me; there is a lot of black, anxious, depressed time to fill; I try to play the piano, I try to read, I try to compose. Mostly, I hide. But maybe hiding isn't so bad. I can't say my mind is any less tangled. I struggle with coherence. I imagine my body would like to stop. Poor abuse receptacle. Like a dog with shit on its arse I'll stumble through the next while not sure why it seems everyone's looking at me.
>
> I think I might miss what I've lost on Tegretol. My fingers don't work on the keyboard; my mind is blank

---

[56]At this point one might argue that my attitude is totally self-centred: I am considering only the benefits of certain mood states for myself, not the negative effects they may have on others who have to live with them. This is true. I do think there's a point at which one's own concerns come first, and this is mine.

[57] This was not the case for instance with Kay Jamison, whose manic episodes were so severe and so frequently psychotic that she endured horrific side-effects from lithium (like not being able to read) for years, until her dosages were straightened out. In her case the manias were simply too violent and dangerous to be tolerated, and she made a courageous decision to stay on lithium, and still managed to be productive. For the story see *An unquiet mind*. I'm lucky; I doubt if I could display that kind of courage, and fortunately I don't have to—at least not yet. Other manic-depressive writers too have valued their disease: Virginia Woolf notes in her diary (17 February 1931) 'All I like is my own capacity for feeling. If I weren't so miserable I could not be happy'. In her case the strange happiness did not last: she finally committed suicide in 1941.

[58]For a sensitive treatment of this issue from a physician's point of view, see Sacks 1995: 235-7.

> facing a blank composition; words swim; consonants fallen over. There are so few words; I used to be able to think of words. I can't think of the word I'm trying to think of, the one that means I used to Have Words. I don't, not now. Eloquent. I used to be eloquent. That's the word I wanted.
>
> Anyway. I'm going to try and carry on reading.[59]

Emotional distress, at least short of psychosis, may be good for some people, or may allow them to find out new and different and often wonderful things about themselves and the world, to develop a special understanding that can help others, and unlock sources of insight and ideas and creativity that would otherwise remain hidden. Even my mixed, black hypomanias are energising and creative, though they feel horrible to be in.

At any rate, it is crucial that the patient get hold of enough information for an intelligent cost/benefit assessment, and then decide. Doctors can be bullies (even inadvertently, with the best will in the world), but nobody has to submit when their personhood is at stake. You can argue with doctors and finally say No. I have chosen the route of blunted but still frequent recurrence, with occasional catastrophic breakthroughs and occasional (and increasingly long-term) remissions, rather than stability in remission. This was a deliberate choice, made after weighing up the relative disadvantages of illness and 'health'. I decided to opt for less than optimal health, in the physician's normative sense, for the somewhat poisoned benefits of nonoptimal treatment. I appear to have managed to achieve the best of two compromised worlds, and for now that seems good enough.

'Cosmetic psychopharmacology'

The term 'cosmetic psychopharmacology' was made popular in the 1990s by the American psychiatrist Peter D. Kramer. It refers to the increasingly common practice (which he found himself resorting to in his own clinical work) of using antidepressants—especially Prozac—for treating states that did not fall within the standard definitions of 'disorders'. They were rather 'penumbral', as he says, somewhere between disturbances of personality and social functioning of the kind that would normally be handled solely by therapy, and actual 'named' disorders. That is, patients suffering from mild phobic states or compulsions, social inhibition, slight hypothymia, otherwise functioning quite well—but unhappy, dissatisfied with their current lives and relationships, or with aspects of their behaviour. In a number of such cases Kramer found that Prozac would ease these relatively mild symptoms in such a way that the patients would feel that they had got 'their real selves' back, or were 'better than good'. This raised for him the ethical issue of whether such treatment, merely to make people somewhat happier or to change their personalities, not to alleviate the symptoms of a major disease, was permissible. Was it right to use drugs designed for serious afflictions simply to mitigate unhappiness or

[59] She improved somewhat on a different mood stabiliser but her condition is not satisfactory, though her musical abilities have mostly come back. Certain kinds of stability can be bad for you.

dissatisfaction—things we all have to deal with in the course of our lives anyhow? Or even more seriously, to alter a personality so that behaviour could fit more neatly with what the patient desired, to 'remake' it to some degree.

For Kramer this raises a serious moral problem: if drugs can be used to alter personalities in specific and relatively predictable ways, could this lead—if one of those outcomes was highly valued by society—to an oppressive, socially sanctioned normativeness? If Prozac or a similar drug could make one more extrovert or aggressive, would there be pressure for people to 'remake' themselves in this mould, if it could lead to better jobs or social success? But the cases Kramer is disturbed by do have some dysthymia, some subjective distress, which even if not lethal or highly disabling is still distress, rather than mere dissatisfaction with one's present self. Kramer sums this issue up as follows (15):

> Some people might prefer pharmacologic to psychologic self-actualisation. Psychic steroids for mental gymnastics, medicinal attacks on the humors, antiwallflower compound—these might be hard to resist [...] Now that questions of personality and social stance have entered the arena of medication, we as a society will have to decide how comfortable we are with using chemicals to modify personality in useful, attractive ways. We may mask the issue by defining less and less severe mood states as pathology, in effect saying, "If it responds to an antidepressant, it's depression." Already, it seems to me, psychiatric diagnosis had been subject to a sort of "diagnostic bracket creep"—the expansion of categories to match the scope of relevant medications.

Though these fears might seem alarmist, Kramer does make an interesting point with potential social and political implications. After observing what appeared to be a major personality change (for the better) in one of his patients, Tess, who was suffering from various problems but clearly not Major Depression, he reflects (16):

> Tess's progress also seemed to blur the boundary between licit and illicit drug use. How does Prozac, in Tess's life, differ from amphetamine or cocaine or even alcohol? People take street drugs all the time in order to "feel normal." Certainly people use cocaine to enhance their energy and confidence [...] Uppers make people socially attractive, obviously available. And when a gin drinker takes a risk, we are tempted to ask whether the newfound confidence is not mere "Dutch courage."

Perhaps his concern is really not so much with the question of medication *per se*, but rather the different perceptions society (and the law) might have of the status of prescribed as opposed to illegally obtained drugs. The niggling question might be whether by the criteria of use and effect alone the two are truly separable or ends of a single continuum. He continues (emphasis mine):

> [...] it is people from Tess's background— born poor to addicted and dependent parents, and then abused and neglected—who are most at risk to use street drugs. A cynic may wonder whether in Tess's case drug abuse has sneaked in through the back door, whether entering the middle class carries the privilege of access to socially sanctioned drugs that are safer and more specific in their effects than street drugs but are *morally indistinguishable in terms of the reasons they are taken and the results they produce*. I do not think it is

> possible to see transformations like Tess's without asking ourselves both whether street-drug abusers are self-medicating unrecognised illness and whether prescribed-drug users are, with their doctors' permission, stimulating and calming themselves in quite similar ways.

I think this is at bottom a pseudoproblem—at least for the patient. If the two kinds of 'treatment' are in essence indistinguishable, and Kramer finds himself willing to prescribe 'legitimate' drugs, why should this resemblance be problematic? Is Kramer himself indulging in a little pharmacological Calvinism? Why shouldn't we—even if we do not suffer from a serious illness—tweak our moods and reshape our personalities right at the synapse with drugs? Is it in some way more reprehensible to lift one's mood with a pill than by running or other exercise that releases endorphins? Or even to use illegal rather than legal prescribed drugs? Is he saying, as he at first appears to be, that certain effects should only be obtained by non-pharmacological means, and if you cannot do it, then you have to suffer?

To some extent I think he is a bit Calvinistic. But there may be a deeper and more subtle if equivocal point here. If the taking of street-drugs for mood- or personality-altering purposes can be either self-medication or 'abuse', then the same could be true of taking prescription drugs. And in the latter case, if the patient is 'abusing' rather than self-treating, the doctor might become a pusher rather than a healer. So the doctor has the problem (especially in patients with a certain kind of background and vulnerability) of deciding whether he is simply producing and/or feeding an addiction, or treating a disorder. My friend M wrote in response to a previous version of this section:

> A street drug user can be an abuser *or* a self-medicator and *so can a taker of prescription drugs*. If the prescribee is an abuser, it is with his doctor's connivance. Telling the difference is what worries Kramer. He makes no judgement about right or wrong—merely about safety and social context. I also think his discomfort lies in the observation that prescribed drugs are used 'with the doctor's permission'. The prescribing doctor *does* have an ethical responsibility. He has to weigh up the pros and cons of any benefits vs. side effects and also the whole tangled issue of inducing dependency or addiction.

What remains somewhat obscure is the precise difference between 'medicinal use' and 'abuse' (here not in the *DSM* sense but the colloquial one). I am not sure there is always an unequivocal boundary. If I feel dissatisfied with aspects of my undrugged self, and drugs (prescribed or not) make me feel better and improve my functioning, isn't that (whether potential addiction is involved or not) actually 'self-medication'? The difficulty might be, though, as Kramer suggests, deciding how serious a disorder or discomfort has to be before it is within the doctor's remit to prescribe for it, especially if the drugs that might be prescribed have potentially dangerous side-effects. The doctor's aim is 'first do no harm' (in general). Even if *I* am willing to take the consequences, to suffer whatever ill effects my chosen drugs may produce, it may be *ultra vires* for the doctor to contribute to this if the risk seems disproportionate to the disorder. Perhaps it is best (if possible) to relieve the doctor of this burden.

For the patient, however, the question is different. How I achieve whatever state I want

to achieve (as long as I don't rape or murder or kill somebody with my car while achieving it) is surely nobody's business but mine. If chemical mood-tweaking makes life more bearable, allows the achievement of desired or needed cognitive or affective or social states and does no harm to anyone else, there is nothing morally problematic about it.[60] Mood-altering drugs accomplish significant transformations by working on the chemical underpinnings of mood and behaviour, and do it efficiently, if not without danger.

The danger is important to note. Not only can some of the drugs themselves be dangerous, but the more different kinds you stuff yourself with the more interactions are possible. On a complex cocktail of drugs with different effects, things can surface that the package inserts do not warn you about. Neurochemicals generally know what they are doing, because evolution has designed them for that; our crude substitutes can sometimes have drastic effects. Still, speaking now in my depressive *persona*, if you are made that way you might as well take the risk. And for some people of course even the risk itself is pleasurable. This is both because risk-taking is often built into the depressive temperament, and because there is always the chance that you might inadvertently kill yourself in the course of trying to feel better, which saves you the trouble of having to do it deliberately. Almost all of us depressives are under the surface perpetually suicidal, I think, no matter how good our present mood.

At any rate I always feel safer when out of the house with my flask within easy reach, and my tiny *millefiore* pillbox tucked somewhere about my person. If such fussy preparedness and fiddling with mood and behaviour make me feel happier and reduce suffering, I do not see why doctors should object. After all, they are in the business of reducing suffering too.[61] There may however be a limit to the extent to which they should be asked to assist in a patient's self-chosen programme, especially if it is as risky as mine.

Outcome: treatment, remission, relapse and recovery

It is not easy to find a medical consensus on intensiveness and time-scale in the treatment of depression There is a common view that the 'index episode' (the first one the doctor sees) should be treated aggressively, and that there should be a period (usually 6-9 months) of continuation treatment after the symptoms have disappeared (or at least been drastically reduced), followed by

---

[60] On the face of it , I do not think it even matters much what drugs are involved: I do not make the simplistic general equation of 'illegal' with 'immoral', though I see the social dangers in certain street drugs. If by taking an illegal drug I am supporting the Colombian cartels, or helping to generate dangerously paranoid crystal meths users, perhaps my action in supporting the trade to please myself is immoral?

[61] In the letter quoted above, M adds, with reference to this section: 'you are very intellectual , self-analytical, argumentative and sure of your ground, whereas many/most other patients (especially perhaps when depressed) are genuinely more dependent on the doctor's judgement than you are. I think the task for doctors is more complex than you allow because you generalise too much from "doctors and me" rather than "doctors and the whole gamut of possible sufferers"'. This is almost certainly well-taken; I leave it here without comment as part of the general dialogue form that so much of this book seems to have assumed. On the other hand I find it difficult to speak for anybody but myself and people like me since I don't know what it feels like to be one.

an unspecified period of 'maintenance' treatment with medication at lower doses, then tapering and withdrawal. This treatment protocol should, as far as I can see from the literature, usually carry the caveat 'until the next episode'. And this is perhaps the central problem.

In a careful and detailed meta-analysis of outcome-studies, C.F. Duggan comes to the following conclusion (1997:36f.):

> First, even with the most generous estimates, only two-thirds of those treated with either psychological or physical treatments can expect to have a prompt response [...] and a further 15% will fail to recover at all [...] and become chronic.[62] Second, among the successful responders, at least a third will have another relapse while in remission [...] third, for those who recover, another episode is likely in 75% of cases with the same cycle being repeated. Thus, for every 100 patients [...] 66 can expect to respond to treatment and 10-15 will remain chronic. Of the 44 who recover, 33 can expect a recurrence with the cycle being repeated [...] only 11% can expect to progress to recovery and remain well without further episodes. Recurrence in particular is a problem as the illness becomes more autonomous, severe and potentially refractory with each new episode [...]

These rather pessimistic figures support what I have been suggesting all along: that depression is more likely than not to be a chronic (in the sense of either continuous or recurrent) illness, and on-and-off treatment is not the ideal choice. (Though it may, unfortunately, be forced on doctors by the exigencies of health insurance and state medical systems, and patients may choose it for a variety of reasons—see chapter 6.) The result of my own experience and years of reading and talking with psychiatrists (at least of the 'biological' persuasion), can be summarised this way:

> (i) Recurrent unipolar major depression and bipolar disorder are chronic (if often remitting) lifelong illnesses, and should be treated as such. That is, patients should be stabilised (to whatever degree is possible, and/or coincides with their preferences and ability to tolerate medication), and the therapeutic dose of medication continued indefinitely.
>
> (ii) Clearly 'reactive' single episodes of major depression (following bereavement or other traumas), if they are first episodes, should be treated as such, normally for a period of no less than 9 months to a year, certainly for at least 6 months after symptoms have disappeared, or a satisfactory response (if not full remission) is obtained.

But it must be noted that kindling can occur at any stage in the evolution of a depression; and each episode makes subsequent ones statistically more likely. Here is one set of risk predictions (Stahl 2000: 16):

---

[62] By 'chronic' Duggan does not mean 'recurrent', but continuous, e.g. depressive states lasting unchanged for a year or more.

Number of Prior Episodes	*Recurrence Risk*
1	< 50%
2	50-90%
3	> 90%

So if a depression of type (ii) is followed—after remission and without additional stressors—by an 'untriggered' major depression, the illness should probably be assumed to be chronic or on the way, and treated as type (i). In these cases, 'the dose that gets you well keeps you well'.(I have been unable to find the source of this commonplace piece of psychiatric wisdom, but I have heard it from a number of doctors.) In an ideal world this would be the safest approach, and the most likely to forestall further episodes, with their attendant danger of increasing severity and shortened interepisode remission.

There is another advantage to long-term, even lifelong treatment: remissions may become longer over time, and their quality may change, even to the point where new positive affects may return or occur for the first time years after treatment is started, and one's response to positive events may become enhanced. This has in fact happened to me, and almost certainly would not have if I had been treated sporadically, once for each serious episode, and then been off medication during remission. It has been, I think, at least partially the first six years of continuous antidepressant treatment that have got me well enough to write this book, and laid a platform for finding out things about myself and beginning to function more normally, and even led to longer periods of more elevated mood than I had ever experienced. I may still often be depressed and manic at times, but I generally feel better(except of course in breakthrough episodes during remission) than I have at any time in the past decade. Some of this is no doubt due to various important life-events; but I believe that these events would have been unable to do anything much for me without the long-term relative stabilisation and neurochemical rebalancing produced by drugs.

On the other hand, the better I feel the less willing I am to tolerate the side-effects of medication, which raises problems of choice. It would be nice to come off Effexor, which though it works still has, half a decade on, the same side-effects it had at the beginning; but would it be a wise thing to do? There is no doubt that there would be new episodes, of a type that do not occur at present: but just what they would be like, and how much 'better' I really am remain matters for speculation—or empirical testing.[63]

A final word for doctors

I end this chapter with a patient's *caveat* about the notion 'wellness' in this complicated cluster of illnesses. Should treatment always proceed until (if possible) the patient is symptom-free, or

[63] I leave this passage as it was when I wrote it; my subsequent history involved undertaking precisely that empirical testing, and the consequences of that decision are described in the following chapter.

are there cases where the physician should consider palliation to some tolerable degree good enough to count as remission? This surely must depend on what the patient wants, and on the side-effects of the medication or medications that otherwise relieve his symptoms. For example, even if, unlike me, a bipolar patient does not *want* hypomanias, there may be good arguments for allowing them, e.g. in a case where they do not get out of hand, and there is no likelihood of psychosis, but the patient's discomfort is increasing because of excessive and poorly tolerated mood-stabilisation. This seems quite common in bipolars on multiple mood-stabilisers. (I have been frankly horrified by the utterly zonked states I have seen some of my friends in, e.g. on multiple mood-stabilisers, an antipsychotic and two antidepressants—this is a real case.) Similarly, in the case of major unipolar depression, it may be advisable to be content with a state that still shows some depressive signs, if the only solution is medication that will cause anxiety, distressing side-effects, or compromise quality of life in other ways. Even if you do not cure a major depression, turning it into dysthymia can be counted a victory.

As an experienced layman who has deliberately chosen non-optimal treatment both to avoid further pharmacologically-induced distress and to retain the useful aspects of my disease, I have a closing reflection for doctors. Granted, the primary medical imperative is to provide 'optimal' treatment; but the medical perspective often sees 'optimality' solely in terms of reduction or removal of targeted symptoms. Diseases however do not exist *in vacuo*; they manifest in living and feeling patients. The good doctor is a craftsman with justifiable pride in his work, and a laudable desire for the 'perfect cure'; but the patient is also the sentient object of his craft. Sometimes then it might be advisable for the doctor to allow the patient to live with an only partly treated mood disorder—provided some reasonable diminution of suffering and increase in functionality are achieved. This 'imperfect' approach may well be more humane and effective medicine than a heroic regime that leaves the patient more pharmacologically than psychiatrically disabled.