The Chemistry of Happiness

Seroxat rivals Prozac as the world's favourite anti-depressant. But not everyone is smiling.

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For some unfathomable reason, the key episodes often occur in supermarkets. Two years ago, Jenny Stanaway returned home from her work as a cleaner and went for her big weekly shop in Swindon. Not long in the busy aisles, she was struck by a panic attack and an urgent desire to flee. She abandoned her shopping but the attacks persisted. After three or four, she went to her doctor and was told that for a woman of her age, in the midst of her menopause, such events were not unheard of. She was prescribed a drug called Seroxat. 'That was the beginning of the end,' she says. 'If I'd have known what it was, there is no way I would have taken it.'

Ian Allen was in a supermarket in Gloucester when he decided to buy 150 tablets of paracetamol. The sales assistant told him, quite properly, that he was not allowed to sell him anything like that amount. 'But I live miles away,' Allen explained.

'I can't come running here every few days.'

Eventually Allen, who is an eloquent 38-year-old wildlife photographer, persuaded the assistant that he should sell him as much as he wanted.

'Don't tell anyone,' the employee said. 'And don't do anything stupid with them.'

'This was rather ironic,' Allen says now. 'Because that was exactly what I was about to do.'

The brain remains the great unconquered organ of scientific and medical knowledge. Ian Allen is fond of saying that if we knew as little about the workings of the heart as we do about the brain, then nobody would dare to perform open-heart surgery. When the brain malfunctions we are often at a loss to detect why, and we are still groping towards effective treatments. Paracetamol is a blunt tool most often used in the masking of headaches, but Allen's intended use was for suicide. He believes that this was a side effect of his doctor prescribing him a drug known as an SSRI - selective serotonin re-uptake inhibitor - a family of medications once recognised only by the tradename of Prozac, but now also marketed as Seroxat, Cipramil, Lustral, Efexor, Dutonin and Faverin. They are most commonly prescribed as treatments for depression, but each year new applications are being found for them. The molecular shape of the drugs is designed to be highly specific, but they are often prescribed for the most unspecific of symptoms: anxiety, insomnia, shyness, natural sadness following bereavement. The drugs are now so widely used that it is difficult to find any community or large organisation without members who are taking them.

In 2000, just under 12m prescriptions of SSRIs were dispensed by the NHS in England alone, almost 4m more than in 1997. An interesting pattern is emerging

regarding their use, quite aside from the question of why we appear to be getting more depressed and anxious. The majority of those on the drugs believe their lives have benefitted from their complex but still unrefined chemistry, but there is also a growing band of desperately unhappy and angry people who claim the medications have all but destroyed them. Inevitably, many solicitors are now involved, and there is the possibility of class actions directed against the pharmaceutical companies who have made the invention of drugs of the mind one of the top priorities of the new century.

Ian Allen says he was given his SSRI for acute insomnia. 'I was a normal person who very rarely visited my doctor. Within a day of taking the drug I was overcome with what I can only describe as an intense disquiet - the most unpleasant thing that I have ever experienced in my life. Many of my friends said they just didn't recognise me.' He says he went back to his GP the next day and told him that the pills were having devastating effects, and his doctor replied that it was unlikely to be the drug. SSRIs are designed to enhance the brain's levels of serotonin, a substance involved in the transmission of nerve impulses and widely thought to be a key element in the maintenance of a balanced mood. They do not generally take effect for two or three weeks, so Ian Allen carried on taking them. He lost almost three stone in three weeks. After a while his employer sat him down and told him he did not consider him well enough to continue working.

'A lot of time on the drugs you feel nothing, but then suddenly the most minor of things can drive you to the most catastrophic actions. In three months I tried to kill myself on six separate occasions, always with lethal intent. The paracetamol tablets. I tried to gas myself in a car, I tried hemlock. Paracetamol is an extremely unpleasant way to kill yourself. It doesn't kill you instantly, and I was found by someone. I ended up in hospital with liver and renal failure.' The strangest thing is, he says, when he woke up in hospital he really couldn't understand why he'd done it.

Allen's recovery began a few weeks after he came off Prozac last August, and he began a lengthy complaints procedure which has yet to yield him any satisfaction. He claims the medical profession and the NHS have brushed him off, blaming his own underlying psychological imbalance rather than the effects of a drug upon it. This is a dilemma encountered by many of those who have bad experiences with SSRIs: because it is so difficult to measure emotional and other mental states, it is almost impossible to show that a worsening condition would not have occurred without interference. The same, of course, applies to an improvement.

What is clear is that by their very nature, anti-depressants tend to be given to people who are in a vulnerable situation. Jenny Stanaway remembers her doctor telling her that she 'needed a little something' to help her through her menopause. She is 52, and used to enjoy a reasonably active life.

She used to work as a cleaner for 20 hours a week, but has not done so since July 2000, which was when she stopped taking her daily morning dose of 20mg of Seroxat.

Stanaway's problem on the drug - severe headaches - was nothing to the predicament she faced when she came off it. 'After 11 months of it I was still getting very bad headaches and I felt the drug wasn't right. My doctor agreed, and she said to come off it by taking one every other day and then stop, which is what

I did. After four days I went into withdrawal. It started with leg spasms. I had nightmares. Muscle weakness. My balance went.'

She saw the duty doctor, who told her to go back on Seroxat. She did this, but the symptoms continued. After a further month, she says her regular doctor said she was very sorry about the adverse reaction, and that the withdrawal now seemed impossible to stop. She came off the drug completely. 'The past 20 months have been unbearable,' she says. Her husband asks her to try to remember what she was like before that episode in the supermarket. She has been on incapacity benefit since January, but only wants to get back to work. 'No one knows how to do this. People tell me I'll get my balance back eventually, but I'm yet to see it. I feel I need a miracle.'

Towards the end of last year she saw a newspaper advertisement soliciting for victims of medical negligence. The person she called referred her on to Mark Harvey at the Cardiff firm of Hugh James Ford Simey, who was then unaware of the full extent of the problems linked to Seroxat. But now he is, for he has since heard more than 100 other stories.

Harvey has conducted many class action medical negligence cases during his career, beginning with the claims against Eli Lilley, the makers of the occasionally fatal anti-arthritic Opren in the early 80s. He is currently seeking compensation for users of Lipobay/Baycol, the anti-cholesterol drug pulled off the market by Bayer after adverse reactions with other drugs resulted in a number of deaths.

The case of Seroxat is not unexpected, he believes. 'The drugs are all trying to fill that huge gap in the market - covering anything from mild to serious depression - and if you can produce something that alleviates the problems and isn't addictive, then you have a huge winner. People now go to their doctor and say, "But will I be addicted?" because they've all heard the Valium stories.'

The data sheet that accompanies each packet of Seroxat has a bold claim: 'These tablets are not addictive.' A little later in the patient instructions, after information about not taking it with the popular blood-thinning drug warfarin and other medications, the reassuring message appears again: 'Remember that you cannot become addicted to Seroxat.' Many patients now regard this claim as unacceptable.

Mark Harvey says he is still 'shaking the tree' to see how many people are suffering from the sort of severe withdrawal symptoms afflicting Jenny Stanaway. People are learning of his interest at the rate of about two a week. The most common story he hears is that the drug initially worked, but then the difficulties really started. At present he has 120 people on his books, and he has commenced applications for legal aid.

The data sheet supplied to doctors by manufacturers GlaxoSmithKline (GSK) does inform them that withdrawal should be gradual, but Harvey believes that the language employed deliberately downplays the potential problems. 'However you dress it up,' he says, 'they're trying to suggest that it's not a major issue. But I've got people who have been trying to get off it for four or five years and say, "My life is a misery." I've heard this argument about [it not being addictive], but I think it's mischievous. What they're saying is that the body doesn't become so absorbent to the drug that you have to keep prescribing larger and larger amounts. That may well be right. But I have to say that if you're a patient and you

read your information sheet that says "These tablets are not addictive," then they understand that as meaning: "If I want to come off this drug then I should be able to do so without any problems, like coming off penicillin." But to say that there's a technical definition to "addiction" is wrong. It's bad enough doing it to a doctor, but you certainly shouldn't do it to a member of the public.'

Harvey is not the sort of hot-headed litigator we may be familiar with from the movies; he does not distrust Big Medicine per se. He acknowledges that a lot of people benefit from Seroxat, and he has a moderate suggestion that falls well short of any grandiose attempt to have the drug withdrawn. 'If [GSK] were sensible, they would sit down and go, "We don't accept any legal liability but we recognise that we could improve the information that we give to the patient and the doctor."'

People become aware of Harvey's involvement principally through the internet, which has recently developed into a vast arena of anti-SSRI campaigning and sad stories from depressives. Websites cater for all types of anxiety and melancholy, and they provide a self-help community for those troubled by their treatments. On the popular 'HealingWell' site, which caters for all ailments, the diabetes message board had recently attracted 406 postings, and the one for multiple sclerosis 261. By the same day in mid-April, the message board for anxiety and panic disorders had received 8,208 and the depression board 9,392.

The postings have titles like 'In A Deep Hole and I'm Sinking Again'. Some consider how to withdraw from SSRIs, but others have gone beyond that. One recent message from Sally186 said: 'I've had a horrible weekend. Been more and more anxious lately - pending divorce and my mother-in-law is dying and I love her and it's too much like when my dad died two years ago. Started feeling horrible suicidal urges late last week and only stayed out of the hospital when my therapist agreed to call me twice a day to make sure I was OK. I don't want to hurt my children. God help me. If I'm not in chat tonight you'll know where I am. Sally.'

There was an immediate response: 'Dear Sally, Your thinking is all negative. You've been handed your fate - you can turn it into something good. It really doesn't have to be as bad as you are making it.'

Depression is not a modern affliction; indeed, it was recognised as a treatable illness by Hippocrates. But only recently have we begun to diagnose the scale of the problem, and only in our lifetime has medical science been able to approximate its biological causes. The World Health Organisation estimates that depression is soon to become the second leading cause of disability - behind ischaemic heart disease and ahead of road traffic accidents. Extensive surveys report that major depressive illness occurs in 3-10 per cent of the adult population, with the prevalence in women two to three times higher than in men. A report published in 1997 suggests that major depression is prevalent in 2.3 per cent of the UK population, and mild depression in 7.7 per cent. Thirty to 50 per cent of cases are believed to go undetected.

By themselves, these figures mean little, particularly to those who are not depressives themselves. In the past decade a few graphic memoirs have thrown light on the true nature of severe illness, and the one thing they make plain from the start is that they are not suffering with a bad, common case of the blues. The

American novelist William Styron ventured that 'depression' has been devalued, a word that has 'slithered through the language like a slug, leaving little trace of its intrinsic malevolence'. In his peerless book The Noonday Demon, Andrew Solomon gives an unnerving description of being unable to raise himself from his bed to answer the phone; even a journey to the bathroom becomes a multi-step struggle. On a broader plain, 'the first thing that goes is happiness', Solomon explains. 'You cannot gain pleasure from anything... Your mind is leached until you seem dim-witted even to yourself. If you hair has always been thin, it seems thinner; if you have always had bad skin it gets worse. You smell sour even to yourself. You lose the ability to trust anyone, to be touched, to grieve. Eventually, you are simply absent from yourself.'

Even the best literary descriptions do not help the best scientific minds, nor can they explain the ideal balance in treatment between the several types of psychotherapy and the many types of chemical medications. As with all psychiatric disorders, each case of depression must be judged by its own manifestations and causes. Should we, therefore, be suspicious of the voracious marketing of drugs that claim to cure depression, anxiety, panic and post-traumatic stress in one tiny pill? And what should we make of the news that Seroxat has taken over from Prozac as the bestselling anti-depressant on the market, or that the NHS is currently dispensing 60 per cent more SSRI compounds in England than it was four years ago? Should we be worried, or should we be grateful?

In September 1959, a gathering of many of the world's leading psychiatrists met at Clare College, Cambridge, for a seminar on the treatment of depression. The timing was propitious; new drugs were just emerging from the shadow of tranquillisers such as diazepam (Valium) and chlorpromazine, and the ruthlessly effective and perilously toxic treatment for manic depression, lithium carbonate. The new drugs received only the most cautious welcome from the massed Freudians and Pavlovians, many of whom had not yet learnt to welcome a biomedical aspect to their work.

The principal concern was that the research data that accompanied the launch of new drugs was inconsistent both in its results and methodology: there was inadequate classification of what sort of depression was being treated - one document listed 19 subdivisions of mood - and the improvements shown were vague. On average, the success rate for antidepressant drugs in controlled studies stood at 25 per cent.

There were two new types of chemical remedies under discussion, both relying on the unproven but much-believed theory that mood changes are caused by the imbalance of certain chemicals in the brain called neurotransmitters. These substances - serotonin, dopamine and noradrenaline among them - help send electrical signals from one nerve cell to another. The absence or over-abundance of these chemicals have different effects not only on mood but also on nerve function (a deficiency of dopamine in a specific area of the brain, for example, is the principal cause of Parkinson's disease). Of the two types of drugs that emerged in the late 50s, MAOI drugs (monoamine- oxidase inhibitors) were stimulants, and worked on boosting the levels of neurotransmitters in the

bloodstream. They had a devastating side effect, causing a life-threatening increase in blood pressure if combined with the chemical tryamine, which was present in cheese, meat and red wine.
The second group, known as tricyclics on account of their three-ring molecular make-up and most commonly available under the name of imipramine, were mild sedatives, and blocked the re-absorption of the neurotransmitter norepinephrine into certain cells, thus extending its life. Throughout the 60s, both MAOIs and tricyclic treatments were refined and slightly improved, although their limitations were apparent to all who prescribed them and many who swallowed them. Pharmaceutical companies launched new molecular twists onto the market with tradenames such as Nardil and Parnate, but their social impact was seldom acclaimed beyond the walls of the firms that made them.
In the middle of the 70s, reports of a new breed of antidepressant began emerging from small laboratories in Scandinavia. It was found that certain drugs like reserpine, a popular tranquillizer and anti-hypertensive treatment that depleted serotonin levels had an interesting side effect: it produced depression-like symptoms.
At the Danish firm of Ferrosan, the head of research was a man called Jørgen Buus Lassen, who supported the theory that the specific enhancement of serotonin might lift a depressive mood. He tested about 100 compounds before deciding on one that became known as paroxetine. 'We did all the clinical trials,' he says today from his office in Glostrup, near Copenhagen, 'and what created most excitement among our scientists was that in some trials we saw that some patients who had been totally hopeless on the existing drugs and not at all responsive to treatment, were gradually becoming better and better. Some who had been unable to work for several years and had been in and out of psychiatric hospitals gradually came into normal life again.'
Dr Buus Lassen's first paper on paroxetine was published in 1975, and it was frank about the drug's limitations. 'It didn't work with all patients,' he remembers. 'In most studies we could just show that we had about the same efficacy as the older tricyclic antidepressants. We didn't see a better effect, but we saw fewer side effects [mainly nausea].'
The work at Ferrosan came to the attention of Beecham, which was then best known for its antibiotic Amoxil, and the two established a partnership for further trials and marketing. The companies were supported in their research by Dr Arvid Carlsson at Gothenburg University (who subsequently won the Nobel Prize for his work on dopamine), and the principle behind paroxetine was mirrored in the other SSRI compounds that began emerging from other companies. The drugs acted to block serotonin being reabsorbed back into the nerve cell after it had transmitted an impulse across a synapse, thus increasing the amount available to be absorbed by the next cell and theoretically enabling 'message transmission' to return to normal.
Dr Buus Lassen says that he knew most of the researchers at the other, competing companies, and remembers no great rush to market. Trials of antidepressants are particularly tricky to conduct, because it's extremely difficult to document improvements in a patient's condition and set this against the reaction to other treatments. A novel tool for measuring a depressive state - a survey with

questions such as: 'Have you wanted to cry? Do you feel beyond tears?' - was developed by Professor Max Hamilton, who worked in close collaboration with Ferrosan and Beecham. It has since become a classic psychiatric questionnaire.
With regard to side effects, Dr Buus Lassen observed 'some nausea, some gastrointestinal disturbances but not severe ones, but we didn't treat patients for an extremely long time. Most of our studies were six, eight or 10 weeks, and we didn't really see withdrawal symptoms from being very different from those in placebo. But it was not within the clinical programme to elucidate if [withdrawal symptoms] occurred after two years.'
One unexpected effect of the drug hastened the pace of its production: it was found very difficult to take a fatal overdose. Clearly, within the field of antidepressant drugs, this is a distinct advantage. 'Gradually,' Dr Buus Lassen observes, 'the market expanded and expanded and expanded.'
But the first drugs on the market showed disturbing traits. Ferrosan and Beecham were beaten to production by the rival firm of Astra, whose SSRI zimelidine appeared in the mid-80s. But when it was tested in the UK a few patients developed a serious auto-immune condition damaging peripheral nerves, and it was discontinued. The same fate befell a drug produced in France called indalpine, which was thought extremely effective until damage was detected to blood-cells. For a while it seemed SSRIs were far from the safe compounds that their designers had wished for.
The first successful launch was of a compound called fluvoxamine, which has the trade names Faverin and Luvox. But the next launch was more significant. Eli Lilley launched fluoxetine in 1987, and under its tradename of Prozac it became an emblematic product, a happiness pill that became a panacea for the world's ills. Alongside Viagra, it was a media sensation and a marketeer's wet dream, a true wonder drug. As with other SSRIs, Prozac was regarded as safer than its predeccesors, but it wasn't long before negative stories began appearing. Patients reported nausea, sexual dysfunction, dependence and violent behaviour, and the drug soon became a symbol of something else, the me-generation desire for the quick fix, for a medical solution for a deeper malaise.
Paroxetine had a less immediate impact, but it would benefit from the Prozac backlash. It assumed the tradenames Seroxat in Europe and Paxil in the US, and was launched in the UK, its first market, in 1991. It has now been prescribed 100m times in more than 100 countries. Beecham is now part of GSK, the world's second-largest pharmaceutical company, boasting a pre-tax profit in 2001 of £6.2bn. In 2000, sales of Seroxat/ Paxil were valued at £1,550m, a 17 per cent increase on the previous year, and the drug ranks in one of GSK's top six performers alongside Avandia for diabetes and Flixotide for asthma.
Part of this success is the way it has been aggressively marketed to doctors (and in the US, directly to patients). One campaign, aimed at healthcare purchasers, came complete with a twopence coin and the sort of knocking copy that pervades this lucrative and highly competitive industry. It read: '2p or not 2p - That is the question. Treating a patient with everything that Seroxat 20mg has to offer, will cost just 59p a per day. Or, you could save a whopping great 2p a day by prescribing [a generic rival] citalopram 20mg. But then, they would not be getting Seroxat, would they?Any further questions?'

As with most drugs, Seroxat usually hits the headlines when the news is bad. Recently there have been a lot of headlines. In June 2001, GSK were ordered to pay $6.4m to the family of Donald Schell, after a jury in Wyoming heard that he had killed his wife, daughter and granddaughter and then himself after two days on Seroxat. The company is appealing the award, claiming that this was a tragedy caused by severe depression, not its treatment. According to one expert witness at the trial, Dr David Healy, director of the North Wales Department of Psychological Medicine, documents released in the discovery process reveal that early studies on SmithKline Beecham's own staff indicated withdrawal symptoms of agitation and insomnia after only a short period on the drug. In 1999 the World Health Organisation published a study which placed Seroxat at the top of a list of drugs which doctors believe cause marked withdrawal problems, with twice as many complaints as the next drug, another SSRI compound. And last month a study at Birmingham University suggested that SSRIs may promote certain types of cancer by blocking the body's natural ability to destroy diseased cells.
GlaxoSmithKline is based at Brentford in Middlesex, but its psychiatric drug research unit is in Greenford, near Harrow, which is where, in the middle of what had been officially designated Mental Health Week, I visited Dr Raj Kumar, the company's worldwide head of Psychiatry for Clinical Development and Medical Affairs. Dr Kumar is 44, and since he joined Beecham 12 years ago he has been responsible for finding several new uses for paroxetine. These include panic disorder, social-anxiety disorder, post-traumatic stress disorder, and obsessive-compulsive disorder. All these new applications have helped to distinguish the drug from its six competitors, and to boost its sales. His group also devised the clinical programme for Seroxat in Japan for the treatment of depression, where it was launched in November 2000, despite the fact that linguistically there's no such word as depression in the Japanese language.
He says he finds it very satisfying to be able to give a community Seroxat, because it has a marked effect on their quality of life. 'It creates the buzz of people saying, "Let's go and look for the next better thing."'
I asked him how he reacts when he reads about the negative comments from patients. 'First,' he said, 'there's no clinical evidence for addiction. Secondly, Seroxat has gone through the regulatory and review processes in Japan and America and almost every major country in Europe. And they've all been happy with the data that we've provided. And then you look at the millions of patients who have used them - most of them are positive and benefit from the drug. It's only individual physicians who are treating patients who must ask, "Do those adverse symptoms exist?", and it is those physicians who must manage those issues.'
This was an intriguing answer, one that appears to dismiss all responsibility for Seroxat's undesirable after-effects . But he did then postulate that the drug might be far from ideal in its present form. 'If I was designing a new antidepressant there might be a whole host of things I'd wish to overcome, but the important thing is, does it work as an antidepressant? The other question is, are the side effects limiting and debilitating, or can the patient tolerate them because the risk/benefit ratio is such that it's better to get an improvement for the depression?'

Dr Kumar says GSK has several new compounds in various stages of clinical trials, each designed to improve on what there is now. This looks like part of what the Harvard Medical School psychiatrist Joseph Glenmullen has defined as the '10-20-30' cycle: a new drug appears and some problems with it are noted within a decade; the manufacturer denies these for a decade more; not long afterwards, after the patent has expired and profits have declined, it produces something it claims to be superior. But even after 30 years, the full impact on SSRIs on the brain may not be known.

Dr Kumar says he gets lots of positive feedback, particularly from the US, from patients saying how Seroxat has transformed their life. 'What they really appreciated was being given more information on how the drug was to be used... and being told what would work for them and why. Very appreciative. Many letters.'

Satisfied customers are indeed not hard to find. One colleague told me that he takes an unusually high dosage of 60mg per day (the norm is 20 or 30mg), which costs him £94 a month for his private prescription. He started taking it last August, after having what psychiatrists tend to call 'negative thoughts'.

'I was feeling suicidal. I hadn't actually made any plans, but I was very very down, very negative about most things, even the most trivial. Very small things would become big problems.' The Seroxat took a long time to work for him (10 to 12 weeks), but then he noticed a distinct improvement. 'I became far calmer and laid-back about things and I was much more content. Now, back at work, I feel as if I'm a slightly different person. People keep noticing that I'm much more talkative and I'm much more outgoing. But I'm not sure if that's a result of the medication or me just learning from my experience and trying to correct my past behaviour.'

A similar dilemma afflicts Lewis Wolpert, professor of Biology as Applied to Medicine at University College, London and author of Malignant Sadness: the Anatomy of Depression (Faber), a book in which he relates his personal battle with depression and analyses the causes and treatments of the disease. His observation that his depression felt worse even than watching his wife Jill Neville die of cancer caused much disquiet, but he maintains the notion that unless you have suffered from it, it is impossible to describe how it feels.

Shortly after admitting to suicidal tendencies in the mid-90s he was hospitalised for three weeks, and his psychiatrist prescribed Seroxat. He has nothing but praise for the drug, believing it may have saved his life. But he also admits to a great paradox: he has no way of knowing whether it actually works at all.

Since his first major depression when he was 65 he has had several other less devastating ones, and on each occasion he has turned to Seroxat for recovery. When I talked to him a few weeks ago he was taking a low dosage every morning, and had no desire ever to come off the drug again.

'People say to me, "Is the Seroxat helping you now?" But how the hell can I know? Maybe I would have got better anyhow. It doesn't do much for your sex life, that I can tell you. And maybe it caused the nausea I had. But that's the only price I pay. I stick with it because I'm too nervous to stop. I'm not addicted to it in any way whatsoever. When I came off it in the past I was fine. But the likelihood is that I will have another episode at some point, and I'm not prepared to take the chance

of coming off it.'
I suggested that only if he came off it would he know how helpful it was being.
'Oh no,' he said in a sombre tone. 'Oh no. Oh no. Only someone who was not a depressive would say that. I'm terribly sorry. Maybe it makes me at times slightly manic, but thank God.'
Professor Wolpert has little time for negative comments about Seroxat, and jokes that if Seroxat grew on trees everyone would be happy to take it.
'I can't tell you how many psychiatrists and other people I know who are on Seroxat, but it's a lot, and they all feel it's helped.'
Jørgen Buus Lassen, the man who did more than anyone to create Seroxat, is now president and CEO of Danish biotechnology company NeuroSearch. His company is developing exciting new compounds for Alzheimer's and brain damage following stroke, but it is also working on new antidepressants. The aim now is to find something that will have a beneficial effect in a few days rather than a few weeks, possibly by working on blocking the reuptake of two or three neuro-chemicals rather than one. He and his colleagues are still working with GSK, and recently their partnership suffered a setback. An antidepressant drug called NS2389/GW650250A has been in development for several years, but was abandoned last month after abnormal cell growth was observed in experiments on rats and dogs.
Other antidepressants are still the cause of optimism. Dr Buus Lassen talks of early clinical studies that suggest a newer, multi-neurotransmitter approach works on some patients who do not respond to serotonin enhancement alone (these compounds are called mixed monoamine reuptake inhibitors, or MMRIs).
'But we still have to learn and see if this is right,' he says. 'Until we've had a full programme, it's still a kind of prediction. We have many pieces, but we don't know why not all patients are being cured. Several pieces we do not understand.'
At the current rate of progress, this new generation of treatment may appear in 2006, which will be timely for GSK, for this is the same year as its patent expires on Seroxat. For the time being we must contend with chemistry that is both impure and uncertain, and prototypes for a perfect drug that we may never see.
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www.depressionalliance.org

www.psychologyinfo.com/depression