Suddenly losing your sense of smell can remove all pleasure from food and drink. Doctors say it’s untreatable, but Mick O’Hare didn’t take no for an answer.

ONE Friday in June 1998, I sat down with a curry for a self-indulgent night watching the soccer World Cup on TV. I had no idea how my next words would signal a momentous change in my life: “I can’t taste anything,” I told my wife.

She pointed out that I had a cold. True, I had struggled through the week with a dreadful sore throat, and by now the infection had spread to my nose and sinuses. But I knew immediately that my problem wasn’t simply the nasal congestion that everyone suffers now and then with a cold. It was a total absence of any sense of taste or smell.

I spent the next week sniffing everything from herb jars to dog muck: nothing. It was terrifying. As someone who loves food and drink, my life had been turned upside down in an instant. My wife and I were enthusiastic cooks – we even planned holidays based on local cuisines and took wine-tasting classes – and I was a member of CAMRA, the UK’s real ale club. It was all suddenly meaningless.

My general practitioner’s advice was less than encouraging. Like most GPs, she had no experience of my situation and could offer no helpful advice. Wait and see, was all she could say. So as many patients do, I hit the internet. I found the names of my afflictions: I had become ageusic, lacking a sense of taste, and anosmic, lacking a sense of smell.

I quickly realised that the anosmia troubled me more. Most of what we call taste is actually flavour produced by the smell of the food passing into our nasal cavities. True taste is only the bitter, sweet, salt, sour and “umami”, or savouriness, detected by the tongue’s taste buds. Bite into a strawberry and your tongue only tells you that it is sweet; it is the odours rising through your throat to your nose that tell you that particular sweetness is strawberry-flavoured.

I discovered the truth of this when, over the next couple of months, my sense of taste gradually returned. The bitterness of green peppers and the sweetness of chocolate began slowly to seep back. Yet agonisingly, smell and flavour remained entirely absent.

At my insistence, my GP referred me to a succession of ear, nose and throat (ENT) specialists. Their verdict was devastating: I had to live with it. My sense of smell – and with it, everything from the faint flavour of lettuce to the fierce assault of piri-piri chicken – had probably gone forever.

In desperation I continued my internet research. I discovered that while estimates vary, it is thought that anosmia affects about 0.66 per cent of the population in the US. Head injuries cause more than a third of cases, and cold and flu viruses account for about another third. Other causes include chronic sinus infections and nasal polyps.

I started to learn more about the sense I had taken for granted all my life. Our sense of smell, or olfaction, arises in a small patch of tissue high in the nasal cavity known as the olfactory epithelium (see Graphic, page 44). This contains about 50 million nerve cells, or neurons, that each bristle with minuscule hairs, or cilia, extending into the surface mucus. Airborne molecules that waft up the nostrils and dissolve in the mucus bind to receptor proteins on these cilia, triggering an electrical impulse in the neuron. The signal travels up to a kind of relay station called the olfactory bulb, just behind the olfactory epithelium. Further neurons, bundled together to form the olfactory nerve, pass these signals on to the brain.

Just how this system allows us to distinguish thousand of different smells was only discovered in the 1990s, in work that last year earned the US researchers, Richard Axel and Linda Buck, the Nobel prize for medicine. They discovered that each neuron in the olfactory epithium makes just one type of about a thousand possible receptors. Each receptor is activated only by a specific odour molecule. Every odour produces its own characteristic pattern of firing neurons, which builds up the picture of the smell we experience, as if each odour has its own combinatorial bar code.

So what disrupts this system in anosmia? The standard medical opinion is that viral anosmia like mine, is a result of a cold or flu...
actually hear the soaring wonder of Beethoven’s ninth symphony, would you tell them they can at least watch the musicians pressing valves and waving bows? Nobody would be so insensitive. Yet that is how it is for an anosmic invited to dinner. “It sounds trivial and amusing, but it’s devastating,” one fellow sufferer told me soon after my condition arose. “Yet it’s the only disability where people laugh in your face when you tell them you have it.”

My options seemed to have run out.

Then, about eight months later, I encountered Richard Firsten of Miami on an anosmia web forum. He had had symptoms identical to mine, yet he was apparently virus destroying olfactory epithelium neurons and damaging the cilia on any remaining ones. In rare cases the virus may also damage the olfactory nerve.

Alarmingly, a study by Thomas Hummell at the University of Dresden in Germany has shown that only a third of viral anosmics recover spontaneously. “If the damage is too great, the loss is permanent,” says Tim Jacob, an anosmia researcher at Cardiff University in the UK. “Currently, the standard belief is there is no effective medical treatment.”

As a future without flavour or smell beckoned, the sense of despair grew. I would wake at night consumed by the fear of never again tasting my mum’s Yorkshire puddings or my wife’s chocolate mousse. I began to dread eating. All I could experience was the colour and texture of the food while everyone else commented on the delicious flavours. And meals came round with agonising regularity, three times a day. They are unavoidable, because if you don’t join in, you die.

The thought of meeting friends in a social setting – which always, but always, involved a meal or a drink – meant I would find an excuse to decline invitations. But few people seemed to understand. Would you ask a deaf friend to a concert by the Royal Philharmonic Orchestra? And then, when you remember they can’t actually hear the soaring wonder of Beethoven’s ninth symphony, would you tell them they can at least watch the musicians pressing valves and waving bows? Nobody would be so insensitive. Yet that is how it is for an anosmic invited to dinner. “It sounds trivial and amusing, but it’s devastating,” one fellow sufferer told me soon after my condition arose. “Yet it’s the only disability where people laugh in your face when you tell them you have it.”

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was not on the olfactory epithelium or nerve, but on something else. Henkin began to look at the structures that interacted with the epithelium, and this led him to the serous glands, which are located throughout the surface of the nasal mucosa. These glands produce the nasal mucus that bathes the olfactory epithelium. This was already known to contain a number of substances such as enzymes and growth factors. Henkin began to speculate that the lasting damage done by the virus was actually to the serous glands, altering the composition of the mucus. Previous work by Henkin and others on cells grown in the lab had shown that the olfactory stem cells only grew and divided in the presence of nasal mucus, presumably because of the chemical growth factors it contained.

In the 1970s, Henkin started looking for these growth factors in nasal mucus. He concentrated on a small molecule called cyclic adenosine monophosphate (cAMP), which was known to act like a growth factor on nerve cells such as spinal cord neurons. Henkin measured levels of cAMP in the nasal mucus of viral anosmia patients. The results were intriguing. In patients with partial smell loss, or hyposmia, cAMP was lower than normal. In those with total loss, like me, it was lower still. The correlation was stark: the worse the smell loss, the lower the mucus cAMP (The FASEB Journal, Vol 16, p A1153). Henkin concluded he had probably found the growth factor he was looking for. “Slowly, it clicked,” he says.

Henkin’s next task was to turn this finding into a treatment. He realised an existing medicine called theophylline might fit the bill. It had been used for decades to treat asthma because its main action is to open up the airways, but one of its other effects is to inhibit an enzyme called phosphodiesterase, which breaks down cAMP. So if someone’s serous glands were still producing a small amount of cAMP, theophylline treatment should help it hang around for longer, thus boosting levels of cAMP.

In 1977 Henkin began treating the first few anosmia patients with theophylline, selecting...
Healthy volunteers. Beforehand, the patients before and after the treatment, and also on magnetic resonance imaging on the patients, he had carried out brain scans using functional objective confirmation of this result, because improvement. Henkin had, however, obtained four patients in the study, three had reported clinical trial of theophylline treatment. Out of those who had failed to respond to any other form of treatment and who had low levels of cAMP. Within weeks many began to report improvements, to varying degrees. “If a patient naturally made little cAMP before their virus, it takes longer for theophylline to increase cAMP to the levels necessary to stimulate the stem cells,” says Henkin. In some theophylline had no effect, presumably because their serous glands no longer produced any cAMP.

Henkin continued to offer theophylline to the patients who came to his door, but he could not get funding to carry out a proper randomised controlled trial to compare theophylline with placebo. Drug firms were not interested in such a rare condition. “The companies do not feel that this old and common drug has much in it for them,” Henkin says.

**Smelling the coffee**

By the time I turned up in 1999, although Henkin had published numerous papers on the possible mechanisms behind smell and taste disorders and how theophylline might increase cAMP levels, he had only published one small clinical trial of theophylline treatment. Out of four patients in the study, three had reported improvement. Henkin had, however, obtained objective confirmation of this result, because he had carried out brain scans using functional magnetic resonance imaging on the patients, before and after the treatment, and also on healthy volunteers. Beforehand, the patients showed much less activity than the controls in several areas of the brain that normally respond to smell. After treatment, the three who responded to theophylline showed increased activity in those brain areas, but the non-responder didn’t (Journal of Computer-Assisted Tomography, vol 22, p 760).

So should I go ahead with the treatment? Because I couldn’t spend the rest of my life anosmic and wondering “what if?”, there was simply no other option.

At first progress was slow. But within four months, hints of smell began to return. Early one morning as the coffee brewed at work, I recognised something that had been missing for more than a year. I could barely contain my emotion. By the time the week was out I had smell perfume, tar setting on the London streets and herbs emanating from the local pizzeria – all muted, but present. It was another 18 months before I was back to normal, but once I knew I was on the road to recovery, my feeling of relief and my new-found appreciation of my returning sense was overwhelming.

But Henkin’s work has not become mainstream medical opinion. Bruce Jafek, professor of otolaryngology at the University of Colorado in Boulder, for example, agrees viral anosmia may well be caused by problems with regeneration of the olfactory epithelium, but says it is unclear whether this stems from changes in the mucus.

Theophylline is not approved for the treatment of anosmia, and in the absence of a placebo-controlled trial, it is unlikely to be widely accepted as such. And while it is generally considered a safe drug, it can cause side-effects similar to those of caffeine, such as agitation, headaches and gastrointestinal problems. At higher doses it can be positively dangerous, and can interact badly with other drugs such as the antibiotic ciprofloxacin.

“The use of theophylline is not proven,” says Jafek. “And the treatment has yet to be replicated by other researchers.” He acknowledges, however, that “theophylline has been used safely in asthma treatment for years, so is not, if administered correctly, hazardous”.

Henkin has still not gained funding for a trial, although he is preparing a paper reviewing 230 patients who have received theophylline at the clinic over the last 10 years. This will report that 70 per cent experienced significant improvement, which is certainly higher than the spontaneous recovery rate of 33 per cent seen in Hummell’s study. But then again, that figure may have been an underestimate, because people who suffer a temporary bout of anosmia are less likely to report it to their doctor. Only a formal trial would give us the true picture.

Henkin also reports that out of those who responded to theophylline, about a third have been able to stop treatment without regressing. Another third, however, found that their sense of smell diminished, although resumption of treatment restored it. The remaining third have not attempted to stop treatment.

I am in that last group. I know my recovery could have been a coincidence, but I am ecstatic that I can once again appreciate every smell, however nasty, and every meal, however ordinary. Of course, no two people are alike – we all have different ideas about what constitutes nectar from the gods – but here are some of mine: a pint of Black Sheep ale, my grandmother’s beef and potato pie, newly mown grass, a glass of Rioja, fish and chips from my home town of Cleckheaton, Serrano ham, freshly oiled cricket bats, roasted peppers, stilton cheese, my wife (these are in no particular order, you understand), my son... I could go on and on.