It is now more generally accepted that the pathogenesis of schizophrenia is multifactorial – like other major diseases such as coronary heart disease – with environmental and genetic factors playing a significant part in determining whether a person may exhibit clinical symptoms.

A number of susceptibility genes – 62 at the time of Professor Murray’s Lecture – have been identified, each increasing the risk of schizophrenia by a relatively small percentage, but resulting in clinical symptoms in those unlucky enough to have a sufficient loading of the genes. In around 5 per cent of people with schizophrenia, so-called copy number variants have been linked to the duplication or deletion of genes known to be involved in neurodevelopment. These individuals share the characteristic loss of key genes with people who develop autism, learning disability and other developmental conditions. But it is not yet understood why the loss of the same neurodevelopmental genes may result in autism rather than schizophrenia, for example.

Environment seems to play a significant role in the development of schizophrenia too, particularly social factors. The AESOP study showed that rates are around three times higher in London than in Nottingham or Bristol, for example. Social isolation may play a part. In Italy, where in around 90 per cent of families several generations tend to live together, rates of psychosis are around three times lower than they are in London, where several generations are found living together in only around one in four families. Migration is another factor associated with increased risk of psychosis.

From a biological perspective it is known that dopamine dysregulation is at the root of the pathogenesis of psychotic symptoms. That would explain why dopamine blockers can still help even where social factors are implicated in symptomatology.

Treatment-resistant patients may have a greater degree of neurodevelopmental abnormality than those who respond to treatment. That in turn may be associated to a greater extent with dysfunction in the glutamatergic system, which is also linked to psychotic symptoms.

The Schizophrenia Commission

The potential role of environmental and societal factors in the development of schizophrenia were explored as part of a year-long enquiry by the Schizophrenia Commission, established by the charity Rethink Mental Illness. The Commission set out to examine the current state of care, support and quality of life for individuals with schizophrenia and their families and then, based on its findings, to identify priority actions that would enable peo-
people with schizophrenia to fulfil their potential through improved outcomes.

The Commission, which received 2500 responses, revealed that people found medicines to be among the most helpful treatments. Peer support and cognitive behavioural treatment were also popular. Early intervention teams were very much liked by patients. There may be a number of reasons behind this, including the fact that they are better funded so may attract the more able nurses. But the main reason may be that they are more holistic and so provide greater continuity of care. Patients do not like being passed from team to team and having to repeat their stories over and over.

Results from the Schizophrenia Commission survey showed that some inpatient units were profoundly anti-therapeutic – nobody seemed to be in charge, there was a lack of role models for the nurses, and units were stark and unwelcoming. Some units were so bad that nobody would want to be admitted voluntarily, Professor Murray commented. He strongly acknowledged that it was a very difficult job working in an acute inpatient unit, and argued that staff in these units needed greater support; it may be that they should be paid more than other nurses, for example. In addition, even though the nurses make up the vast majority of the staff, they had little chance to go on refresher courses and to learn new skills.

Inpatient units should perhaps be more like those in the Burghölzli Hospital in Zurich, suggested Professor Murray. There patients stay in rooms with ensuite bathrooms, they can enjoy a café and nice gardens and they benefit from the presence of ‘therapeutic’ dogs, which live in and are trained to stay calm when people shout or have an outburst, for example, thus providing comfort to the patients.

In stark contrast, there were NHS Trusts where the standard of care was a disgrace, Professor Murray said. Part of the problem was the apparent disconnection between the Trust board and the services they were responsible for. Trust board members should regularly visit facilities to keep in touch with what is happening so that they understand the issues that staff and patients face and have a clear understanding of the quality of the units they are responsible for. Also it would be a good idea for chief executives to spend 24 hours in a psychiatric intensive care unit. The Francis Inquiry highlighted the problems that can arise when managers are not focused on quality of care but are instead too focused on foundation status, the budget, throughput of patients and ticking boxes.

The situation is not helped either by some of the misconceptions that persist among some of those treating patients with psychosis. For example, it is no longer always the case that people need to stay on medication for life, especially following an acute psychosis.

**Backward step**

Another worrying aspect was that the Kraepelin idea of deterioration had started to creep back in: the idea that schizophrenia is a progressive brain disorder, like dementia. Indeed the Schizophrenia Commission heard from patients who had been told they had a progressive brain disorder at their first consultation.

The idea that schizophrenia was a progressive disease came from brain scans that reveal a shrinkage in cortical volume. But the decrease has been shown to be correlated with antipsychotic dose; equally it may be linked to severity of disease. Adolescents also lose cortical volume. So it is not known whether the loss is detrimental. Stress is another factor: for example, high cortisol is linked to low hippocampal volume.

**Drug abuse**

Substances of abuse have been shown to increase the risk of developing psychosis and there is a good deal of anxiety among patients about these. Khat is thought to increase the risk of psychosis. It contains an amphetamine-like substance – cathinone. Khat led to a spate of internet drugs such as methyl methylcathinone (commonly known as MMCat or meow-meow).

Cannabis use has been linked to an increased risk of psychosis. The Dunedin study, for example, showed a four-fold increase in the risk of psychosis, which may be linked to duration of use or susceptibility of the teenage brain. Skunk with its higher tetrahydrocannabinol (THC) (16 per cent) content is associated with a greater risk of psychosis than other forms, which contain lower percentages (4-5 per cent) of THC.

**The future**

Cannabis use in the UK has decreased so it may be that educational campaigns such as Talk to Frank have given young people the information they need to understand the risks of drug abuse and perhaps choose not to indulge. Professor Murray said he felt that the current generation of teenagers seemed to be more sensible than their parents because rates of cannabis use and alcohol consumption have been falling in recent years.
‘It would be great to get to the point where we are at least as concerned about what we “put on our brain” as we are about what we put on our face. Perhaps with more education we may achieve that,’ he commented.

A key to improving care in the NHS would be to expand the early intervention model, which offers greater continuity of care and a more holistic approach. What people hate most is lack of continuity of care, Professor Murray emphasised.

In conclusion, a quote from the Schizophrenia Commission stands out. It is again the words of wisdom from Professor Murray himself that shine a light on how things can really be improved: ‘We now need to make sure that everyone is offered the treatments we know work best, delivered with kindness and competence. If we can achieve this, then together we can make the next decade one of increasing recovery for people diagnosed as having schizophrenia or psychosis.’

References